EPA Pesticide Petition No. IN-10526

(2) The veteran was receiving service-connected disability compensation on the date of death;

(3) The veteran would have been receiving service-connected disability compensation on the date of death, but for the receipt of military retired pay or non-service-connected disability pension; or

(4) The Secretary determines the veteran is eligible for a burial allowance under § 3.1708.

(c) *Amount payable.* The amount payable under this section will not exceed the cost of transporting the remains to the national cemetery closest to the veteran's last place of residence in which burial space is available, and is subject to the limitations set forth in paragraph (d) of this section.

(d) *Reimbursable transportation expenses.* (1) VA will reimburse reasonable transportation expenses, including but not limited to the costs of shipment via common carrier (i.e., procuring permits for shipment, a shipping case, sealing of the shipping case, and applicable Federal taxes) and costs of transporting the remains to the place of burial.

(2) A reasonable transportation expense is an expense that is usual and customary in the context of burial transportation, with a corresponding charge that is the usual and customary charge made to the general public for the same or similar services.

(Authority: 38 U.S.C. 2303, 2308)

Burial Benefits: Other

§ 3.1710 Escheat (payment of burial benefits to an estate with no heirs).

VA will not pay burial benefits if the payment would escheat (that is, would be turned over to the State because there are no heirs to the estate of the person to whom such benefits would be paid).

(Authority: 38 U.S.C. 501(a))

§ 3.1711 Effect of contributions by government, public, or private organizations.

(a) *Contributions by government or employer.* With respect to claims for a plot or interment allowance under § 3.1707, if VA has evidence that the U.S., a State, any agency or political subdivision of the U.S. or of a State, or the employer of the deceased veteran has paid or contributed payment to the veteran's plot or interment expenses, VA will pay the claimant up to the lesser of:

(1) The allowable statutory amount; or

(2) The amount of the total plot or interment expenses minus the amount of expenses paid by any or all of the organizations described in this paragraph (a).

(b) *Burial expenses paid by other agencies of the U.S.* (1) *Burial allowance when Federal law or regulation also provides for payment.* VA cannot pay the non-service-connected burial allowance when any Federal law or regulation also specifically provides for the payment of the deceased veteran's burial, funeral, or transportation expenses. However, VA will pay the non-service-connected burial allowance when a Federal law or regulation allows the payment of burial expenses using funds due, or accrued to the credit of, the deceased veteran (such as Social Security benefits), but the law or regulation does not specifically require such payment. In such cases, VA will pay the maximum amount specified in 38 U.S.C. 2302.

(2) *Payment by military service department.* VA will not pay or will recoup the non-service-connected burial allowance for deaths occurring during active service or for other deaths for which the service department pays the burial, funeral, or transportation expenses.

(3) *When a veteran dies while hospitalized.* When a veteran dies while hospitalized at the expense of the U.S. government (including, but not limited to, death in a VA facility) and benefits would be otherwise payable under 10 U.S.C. 1482 and a provision of this subpart B, only one of these benefits is payable. VA will attempt to locate a relative of the veteran or another person entitled to reimbursement under § 3.1702(b) and will ask that person to elect between these benefits.

(Authority: 38 U.S.C. 2302, 2303(b))

§ 3.1712 Effect of forfeiture on payment of burial benefits.

(a) *Forfeiture for fraud.* VA will pay burial benefits, if otherwise in order, based on a deceased veteran who forfeited his or her right to receive benefits due to fraud under § 3.901, Fraud. However, VA will not pay burial benefits to a claimant who participated in fraudulent activity that resulted in forfeiture under § 3.901.

(b) *Forfeiture for treasonable acts or for subversive activity.* VA will not pay burial benefits based on a period of service commencing before the date of commission of the offense if either the veteran or the claimant has forfeited the right to all benefits except insurance payments under § 3.902, Forfeiture for treasonable acts, or § 3.903, Forfeiture for subversive activities, because of a treasonable act or subversive activities, unless the offense was pardoned by the President of the U.S.

(Authority: 38 U.S.C. 6103, 6104, 6105)

Cross Reference: § 3.1(aa), for the definition of "fraud."

§ 3.1713 Eligibility based on status before 1958.

When any person dies who had a status under any law in effect on December 31, 1957, that afforded entitlement to burial benefits, burial benefits will be paid, if otherwise in order, even though such status does not meet the service requirements of 38 U.S.C. chapter 23.

(Authority: 38 U.S.C. 2305)

[FR Doc. 2014–13230 Filed 6–5–14; 8:45 am]

BILLING CODE 8320–01–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2012–0922; FRL–9910–50]

Sodium Bisulfate; Exemption From the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of sodium bisulfate when used as an inert ingredient in antimicrobial formulations on food contact surfaces in public eating places, dairy processing equipment and food processing equipment and utensils at no more than 2,000 ppm in final formulation. Exponent on behalf of Ecolab, Inc. submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting establishment of an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of sodium bisulfate.

DATES: This regulation is effective June 6, 2014. Objections and requests for hearings must be received on or before August 5, 2014, and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA–HQ–OPP–2012–0922, is available at *http://www.regulations.gov* or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), EPA West Bldg., Rm. 3334, 1301 Constitution Ave. NW., Washington, DC 20460–0001. The Public Reading Room is open from 8:30

a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566–1744, and the telephone number for the OPP Docket is (703) 305–5805. Please review the visitor instructions and additional information about the docket available at *http://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: Lois Rossi, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001; telephone number: (703) 305–7090; email address: *RDFRNotices@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How can I get electronic access to other related information?

You may access a frequently updated electronic version of 40 CFR part 180 through the Government Printing Office's e-CFR site at *http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl.*

C. How can I file an objection or hearing request?

Under FFDCA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA–HQ–OPP–2012–0922 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before August 5, 2014. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA–HQ–OPP–2012–0922, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.
- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.html.*

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

II. Petition for Exemption

In the **Federal Register** of January 16, 2013 (78 FR 3377) (FRL–9375–4), EPA issued a document pursuant to FFDCA section 408, 21 U.S.C. 346a, announcing the filing of a pesticide petition (*PP* IN–10526) by Ecolab, Inc., 370 N. Wabasha Street, St. Paul, MN 55102. The petition requested that 40 CFR 180.940(a) be amended by establishing an exemption from the requirement of a tolerance for residues of sodium bisulfate (CAS Reg. No. 7681–38–1) when used as an inert ingredient in antimicrobial pesticide formulations applied to food contact surfaces in public eating places, dairy processing equipment and food processing equipment and utensils at no more than 2,000 ppm in final formulation. That document referenced a summary of the petition prepared by Exponent, 1150 Connecticut Ave. NW., Suite 1100, Washington, DC 20036, the petitioner, which is available in the docket, *http://www.regulations.gov.*

III. Inert Ingredient Definition

Inert ingredients are all ingredients that are not active ingredients as defined in 40 CFR 153.125 and include, but are not limited to, the following types of ingredients (except when they have a pesticidal efficacy of their own): Solvents such as alcohols and hydrocarbons; surfactants such as polyoxyethylene polymers and fatty acids; carriers such as clay and diatomaceous earth; thickeners such as carrageenan and modified cellulose; wetting, spreading, and dispersing agents; propellants in aerosol dispensers; microencapsulating agents; and emulsifiers. The term "inert" is not intended to imply nontoxicity; the ingredient may or may not be chemically active. Generally, EPA has exempted inert ingredients from the requirement of a tolerance based on the low toxicity of the individual inert ingredients.

IV. Aggregate Risk Assessment and Determination of Safety

Section 408(c)(2)(A)(i) of FFDCA allows EPA to establish an exemption from the requirement for a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is "safe." Section 408(b)(2)(A)(ii) of FFDCA defines "safe" to mean that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." This includes exposure through drinking water and in residential settings, but does not include occupational exposure. Section 408(b)(2)(C) of FFDCA requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue. . . ."

EPA establishes exemptions from the requirement of a tolerance only in those cases where it can be clearly demonstrated that the risks from aggregate exposure to pesticide chemical residues under reasonably foreseeable circumstances will pose no appreciable risks to human health. In order to determine the risks from aggregate exposure to pesticide inert ingredients, the Agency considers the toxicity of the inert in conjunction with possible exposure to residues of the inert ingredient through food, drinking water, and through other exposures that occur as a result of pesticide use in residential settings. If EPA is able to determine that a finite tolerance is not necessary to ensure that there is a reasonable certainty that no harm will

result from aggregate exposure to the inert ingredient, an exemption from the requirement of a tolerance may be established.

Consistent with FFDCA section 408(c)(2)(A), and the factors specified in FFDCA section 408(c)(2)(B), EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure for sodium bisulfate including exposure resulting from the exemption established by this action. EPA's assessment of exposures and risks associated with sodium bisulfate follows.

A. Toxicological Profile

EPA has evaluated the available toxicity data and considered their validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children. Specific information on the studies received and the nature of the adverse effects caused by sodium bisulfate as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies are discussed in this unit.

The acute oral toxicity of sodium bisulfate is low. The acute oral LD_{50} in male rats was 2,800 mg/kg. It was minimally irritating to the rabbit's skin and mildly irritating to the eyes. An acute inhalation study was available with sodium sulfate. Inhalation toxicity was not observed at 0.01 mg/l (the only dose tested). No dermal toxicity or dermal sanitization studies were available in the database.

Due to the lack of data for sodium bisulfate, both human metabolic processes and toxicity data for sodium sulfate were used for the risk characterization. Both sodium bisulfate and sodium sulfate readily undergo hydrolysis and dissociate to sodium ions and sulfate ions in the body.

Sodium sulfate was administered to male Sprague-Dawley rats at a dietary concentration of 0.84% (approximately 320–400 mg/kg/day) for 27 and 44 weeks. There was no mortality, tumors, body weight change or significant changes in food and/or water consumption. The NOAEL was ~320–400 mg/kg/day. In another study, male Sprague-dawley rats were given in diet 0.0, 0.125, 0.250, 0.5, 1 and 2% sodium sulfate (approximately 0, 125, 250, 500, 1,000 and 2,000 mg/kg/day) for 4 weeks. No changes in food and water consumption, body weight gain, food conversion efficiency, urine production or diarrhea. Blood hemoglobin, white blood count, serum alkaline phosphatase, inorganic phosphate and gross organ pathology were also unaffected. The NOAEL was 2,000 mg/kg/day (highest dose tested). A LOAEL was not observed in this study.

Sodium sulfate showed no mutagenic effect in the Ames test using various strains of *S. typhimurium* (TA1535, TA1537, TA100, TA98) both with and without S9 activation.

No carcinogenicity studies were available in the database. The National Toxicology Program (NTP), International Agency for Research on Cancer (IARC), and Occupational Safety & Health Administration (OSHA) have not listed sodium bisulfate as a carcinogen. A DEREK analysis was performed on sodium bisulfate and no structural alerts were detected. EPA concluded that sodium bisulfate is unlikely to pose a carcinogenic risk to humans based on lack of mutagenicity concerns for sodium sulfate, lack of any structural alerts for carcinogenicity, lack of any systemic toxicity at doses up to 2,800 mg/kg/day, and its metabolism to form a sulfate which is natural constituent present in the body.

Sodium sulfate was included in a test of a method for rapid assessment of teratogenicity. Pregnant ICR/SIM mice were given a saturated aqueous solution of sodium sulfate orally by gavage to deliver a dose of 2,800 mg/kg/day on days 8–12 of gestation. No maternal deaths occurred and the average maternal weight gain during the treatment period was not significantly different from that of water-treated controls. Twenty-four litters were delivered alive, and none were resorbed. The mean numbers of neonates delivered alive and dead in each litter and the survival of neonates on day 3 were not statistically significantly different from those of controls. Only body weight on day 1 was statistically significantly greater than that of controls. The maternal and developmental NOAEL = 2,800 mg/kg bw, the only dose tested.

No immunotoxicity, neurotoxicity or reproductive toxicity studies were available in the database.

Sodium bisulfate mammalian metabolism is essentially that of the sodium cation and sulfate anion. As previously noted, when sodium bisulfate is added to food products containing water or after ingestion of sodium bisulfate it ionizes to sodium ions, hydrogen ions and sulfate ions. Following ingestion, sulfate anions are predominantly not absorbed from the gastrointestinal tract and are excreted unchanged in urine. However, the sulfate anion is a normal constituent in the body, predominantly resulting from the body's metabolism of sulfur-containing food sources such as foods containing the essential amino acids cysteine and methionine. Sulfate anions are vital components in a number of human biosynthetic pathways such as cartilage production and the formation of pancreatic digestive enzymes. Additionally, the sulfate anion is also an important conjugate in the Phase II conjugation/elimination of oxidized (OH) aromatic ring metabolites and for hydroxyl steroid hormones, such as estrogen, where it acts as a transport agent to target organ tissue receptors.

B. Toxicological Points of Departure/Levels of Concern

Once a pesticide's toxicological profile is determined, EPA identifies toxicological points of departure (POD) and levels of concern to use in evaluating the risk posed by human exposure to the pesticide. For hazards that have a threshold below which there is no appreciable risk, the toxicological POD is used as the basis for derivation of reference values for risk assessment. PODs are developed based on a careful analysis of the doses in each toxicological study to determine the dose at which no adverse effects are observed (the NOAEL) and the lowest dose at which adverse effects of concern are identified (the LOAEL). Uncertainty/safety factors are used in conjunction with the POD to calculate a safe exposure level—generally referred to as a population-adjusted dose (PAD) or a reference dose (RfD)—and a safe margin of exposure (MOE). For non-threshold risks, the Agency assumes that any amount of exposure will lead to some degree of risk. Thus, the Agency estimates risk in terms of the probability of an occurrence of the adverse effect expected in a lifetime. For more information on the general principles EPA uses in risk characterization and a complete description of the risk assessment process, see *http://www.epa.gov/pesticides/factsheets/riskassess.htm.*

There was no hazard identified in repeat dose developmental studies at the limit dose of 2,800 mg/kg/day of sodium sulfate to either parental animals or their offspring. No effects were seen in two subchronic oral toxicity up to approximately 2,000 mg/kg/day of sodium sulfate. Based on the metabolism of sodium bisulfate to sulfate and sodium ions, both of which are essential components in the human

metabolic processes, there is a lack of toxicological concern. Thus, due to its low potential hazard and lack of hazard endpoint, the Agency has determined that a quantitative risk assessment using safety factors applied to a point of departure protective of an identified hazard endpoint is not appropriate.

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* In evaluating dietary exposure to sodium bisulfate, EPA considered exposure under the proposed exemption from the requirement of a tolerance (40 CFR 180.940(a)) such as food in contact with sanitized counters in public eating places, utensils, dairy processing equipment and food processing equipment as well as other uses which may result in dietary exposure.

However, because no hazard was identified for the acute and chronic dietary assessment (food and drinking water), or for the short-, intermediate-, and long-term residential assessments, no quantitative aggregate exposure assessments were performed.

2. *Dietary exposure from drinking water.* Residues of sodium bisuflate from uses in food contact sanitizing solutions, utensil, dairy processing equipment and food processing equipment may enter drinking water. However, because no hazard was identified for the acute and chronic dietary assessment, or for the short-, intermediate-, and long-term residential assessments as listed in this unit, no quantitative aggregate exposure assessments were performed.

3. *From non-dietary exposure.* The term "residential exposure" is used in this document to refer to non-occupational, non-dietary exposure (e.g., textiles (clothing and diapers), carpets, swimming pools, and hard surface disinfection on walls, floors, tables).

Residential (dermal and inhalation) exposure from food contact surface sanitizing solutions for public eating places, dairy-processing equipment, food-processing equipment and utensils are possible. Since an endpoint for risk assessment was not identified, a quantitative residential exposure assessment for sodium bisulfate was not conducted.

4. *Cumulative effects from substances with a common mechanism of toxicity.* Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA has not found sodium bisulfate to share a common mechanism of toxicity with any other substances, and sodium bisulfate does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that sodium bisulfate does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's Web site at *http://www.epa.gov/pesticides/cumulative.*

D. Safety Factor for Infants and Children

The toxicity database for sodium bisulfate is adequate for assessment of risks to infants and children and the potential exposure is adequately characterized given the low toxicity of the chemical and formation of sulfate ion. No hazard was identified and there is no residual uncertainty regarding prenatal and/or postnatal toxicity. No acute or subchronic neurotoxicity studies are available, but there were no clinical signs of neurotoxicity or any systemic toxicity observed in the available database at doses up to 2,800 mg/kg/day. No developmental, reproductive, or teratogenic effects were seen in the available studies at doses up to and including 2,800 mg/kg/day.

Based on this information, there is no concern at this time for increased sensitivity to infants and children to sodium bisulfate when used as an inert ingredient in pesticide formulations for food contact surface sanitizing applications and a safety factor analysis has not been used to assess risk. For the same reason, EPA has determined that an additional safety factor is not needed to protect the safety of infants and children.

E. Aggregate Risks and Determination of Safety

Taking into consideration all available information on sodium bisulfate, EPA has determined that there is a reasonable certainty that no harm to any population subgroup, including infants and children, will result from aggregate exposure to sodium bisulfate under reasonable foreseeable circumstances. Therefore, the establishment of an exemption from tolerance under 40 CFR 180.940(a) for residues of sodium bisulfate when used as an inert ingredient in pesticide formulations applied to food contact surface sanitizing solutions for public eating places, dairy processing equipment, food processing equipment and utensils at no more than 2,000 ppm in formulation, is safe under FFDCA section 408.

V. Other Considerations

A. Analytical Enforcement Methodology

An analytical method is not required for enforcement purposes since the Agency is not establishing a numerical tolerance for residues of sodium bisulfate in or on any food commodities. EPA is establishing a limitation on the amount of sodium bisulfate that may be used in pesticide formulations. The limitation will be enforced through the pesticide registration process under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. 136 *et seq.* EPA will not register any pesticide for sale or distribution that contains greater than 2,000 ppm of sodium bisulfate in the pesticide formulation.

B. International Residue Limits

In making its tolerance decisions, EPA seeks to harmonize U.S. tolerances with international standards whenever possible, consistent with U.S. food safety standards and agricultural practices. EPA considers the international maximum residue limits (MRLs) established by the Codex Alimentarius Commission (Codex), as required by FFDCA section 408(b)(4). The Codex Alimentarius is a joint United Nation Food and Agriculture Organization/World Health Organization food standards program, and it is recognized as an international food safety standards-setting organization in trade agreements to which the United States is a party. EPA may establish a tolerance that is different from a Codex MRL; however, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

The Codex has not established a MRL for sodium bisulfate.

VI. Conclusions

Therefore, an exemption from the requirement of a tolerance is established under 40 CFR 180.940(a) for sodium bisulfate (CAS Reg. No. 7681–38–1) when used as an inert ingredient in antimicrobial pesticide formulations applied to food contact surface sanitizing solutions for public eating places, dairy processing equipment, food processing equipment and utensils at no more than 2,000 ppm in formulation.

VII. Statutory and Executive Order Reviews

This final rule establishes a tolerance under FFDCA section 408(d) in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled "Regulatory Planning and Review" (58 FR 51735, October 4, 1993). Because this final rule has been exempted from review under Executive Order 12866, this final rule is not subject to Executive Order 13211, entitled "Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use" (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled "Protection of Children from Environmental Health Risks and Safety Risks" (62 FR 19885, April 23, 1997). This final rule does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA) (44 U.S.C. 3501 *et seq.*), nor does it require any special considerations under Executive Order 12898, entitled "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations" (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerance in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*), do not apply.

This final rule directly regulates growers, food processors, food handlers, and food retailers, not States or tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, the Agency has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, the Agency has determined that Executive Order 13132, entitled "Federalism" (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled "Consultation and Coordination with Indian Tribal Governments" (65 FR 67249, November 9, 2000) do not apply to this final rule. In addition, this final rule does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (2 U.S.C. 1501 *et seq.*).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA) (15 U.S.C. 272 note).

VIII. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq.*), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This action is not a "major rule" as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: June 2, 2014.

Lois Rossi,

Director, Registration Division, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180—[AMENDED]

■ 1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

■ 2. In § 180.940, in the table in paragraph (a), alphabetically add the following inert ingredient to read as follows:

§ 180.940 Tolerance exemptions for active and inert ingredients for use in antimicrobial formulations (Food-contact surface sanitizing solutions).

* * * * *

(a) * * *

Pesticide chemical	CAS Reg. No.	Limits
* *	*	* * * *
Sodium bisulfate	7681–38–1	When ready for use, the end-use concentration is not to exceed 2,000 ppm.
* *	*	* * * *

[FR Doc. 2014–13229 Filed 6–5–14; 8:45 am]
BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2013–0654 and EPA–HQ–OPP–2013–0655; FRL–9910–38]

Flutriafol; Pesticide Tolerances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes, amends, and removes tolerances for residues of flutriafol in or on multiple commodities which are identified and discussed later in this document. Cheminova A/S c/o Cheminova, Inc. requested these tolerances under the Federal Food, Drug, and Cosmetic Act (FFDCA).

DATES: This regulation is effective June 6, 2014. Objections and requests for hearings must be received on or before August 5, 2014, and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA–HQ–OPP–2013–0654 and EPA–HQ–OPP–2013–0655, is available at *http://www.regulations.gov* or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave. NW., Washington, DC 20460–0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566–1744, and the telephone number for the OPP

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

May 30, 2014

Carrie Daniels
Exponent, Inc.
1150 Connecticut Ave., NW
Suite 1100
Washington, DC 20036

Dear Mrs. Daniels,

This letter is in response to the request made by Exponent Inc. on behalf of Ecolab for an exemption from the requirement of a tolerance, 40 CFR part 180.940(a), for sodium bisulfate (CAS Reg. No. 7681-38-1) when used as an inert ingredient in antimicrobial pesticide formulations on food contact surfaces in public eating places, dairy processing equipment and food processing equipment and utensils at no more than 2000 ppm in final formulation.

Based on the information provided in your submission for sodium bisulfate, it has been determined that this inert ingredient is acceptable for use as an inert ingredient in antimicrobial pesticide formulations on food contact surfaces in public eating places, dairy processing equipment and food processing equipment and utensils at no more than 2000 ppm in final formulation.

If you have any further questions or comments, please feel free to contact me by telephone at (703)-308-1846 or by email at shah.pv@epa.gov.

Sincerely,

P.V. Shah, PhD, Chief
Inert Ingredient Assessment Branch
Registration Division (7505P)

Recommendation of Division Directors
Negotiated Due Dates

Decision #:	Registration #:	Petition #: IN-10526

☐ *See page 2 for additional registration entries*

Chemical Name: Sodium Bisulfate (CAS Reg. No. 7681-38-1)

Fee Category: I-002 | **PRIA Decision Time Frame:** 10

Submitted by: David Lieu | **Branch:** OCSPP/OPP/RD | **Date:** 05/06/2014

Company: Exponent on behalf of Ecolab

Original PRIA Due Date: 10/18/2013 | **Proposed New PRIA Due Date:** 05/30/2014

Previous Negotiated Due Dates: 11/29/2013 05/06/2014

Is the "Fix" in-house? ☑ Yes ☐ No ☐ n/a | **If not, date "Fix" expected:**

Negotiated Due Date Reason:

Additional Data Required	☐ Product Chemistry	☐ Toxicology	☐ Acute Tox	☐ Environmental	
	☐ Efficacy	☐ Ecological	☐ Residue	☐ Other	
Data Deficiencies	☐ Product Chemistry	☐ Acute Tox	☐ Efficacy	☐ Residue	☐ Toxicology
	☐ Environmental	☐ Ecological	☐ Labeling	☐ Other	☐ Not Submitted
Late Risk Assessment	☑ Human Health	☐ Ecological			
Interim Consideration	☑ Agency Initiated	☐ Registrant Initiated			

☐ CSF	☐ Public Process	☐ Risk Issues Environmental	☐ Risk Issues Human Health
☐ Impurities Review	☐ Label	☐ Administrative-FR Notice	☑ Other – Comment Field

Summary of Deficiency Type(s): ☐ Not Submitted (N) ☐ Deficiencies (D)

Product Chemistry: ☐ **Acute Tox:** ☐ **Efficacy:** ☐ **Labeling:** ☐ **Ecological Data:** ☐ **Other (describe):** ☐

Describe Interactions with Company (describe when contacted and company's response including response to previous negotiated due dates):

US EPA initially identified potential cumulative exposure concerns for sulfites and sulfates which precluded us from being able to complete a risk assessment. The issue was resolved and it was determined that the tolerance exemption could proceed (11/29). Due to limited data EPA had to do literature reviews. Internal and OGC reviews took longer than expected. Currently waiting for FR typesetting.

"75 Day" Letter sent? ☐ **Yes, Date sent** ☑ **No and reason for none?** *Add comments on page 2*

Rationale for Proposed Due Date: Give adequate time for FR encoding and processing.

Registrant notified that this is the last negotiation? ☐ **Yes** ☑ **Not Applicable**

Approve: ☑ | **Disapprove:** ☐

If disapproved, action to be taken:

OD or DOD Signature: *CN=Marty Monell/OU=DC/O=USEPA/C=US* | **Date:** *05/08/2014*

Decision #:	Registration #:	Petition #: IN-10526

Issue(s) (describe in detail):

US EPA inititally identified potential cumulative exposure concerns for sulfites and sulfates which precluded us from being able to complete a risk assessment specific to sodium bisulfate. The issue was recently resolved and it was determined that the tolerance exemption for the specific uses can proceed forward. however due to the amount of time it took to resolve the concern as well as the time needed to publish a final rule int he Federal Register, we will not be able to grant approval of the submission by the original PRIA due date of 10/18/2013. However the registrant wished to set the new due date as 11/29/2013. US EPA agreed to teh registrants suggestion however the registrant was also told we do not believe this would be enough time and that it may be possible that we would have ot renegotiate another due date again. Now with the limited data provided by the registrant, EPA had to do reviews of literautre. Then it was determined EPA did not have enough time needed to complete the risk assessment and that a renegotiation would be necessary. The new date of 05/06/2014 was agreed upon. Then due to longer than expected internal and OGC reviews the final rule was not sent to the Federal Register Staff until last week. This did not give enough time for the Federal Register Staff to encode the final rule and send it back to us. We requested additional time for this process to be completed. The registrant agreed to 05/30/2014 as the new PRIA due date.

Comment(s):

Audit Trail for

Recommendation of Division Directors Negotiated Due Dates

PDF Name: PRIAv5.pdf
Form Number: PRIA
Document Identifier: PRIA-14126130448-DL

SUBMITTED on 05/06/2014 at 01:32:28 PM by CN=David Lieu/OU=DC/O=USEPA/C=US

APPROVED on 05/06/2014 at 01:41:47 PM by CN=Pv Shah/OU=DC/O=USEPA/C=US

APPROVED on 05/07/2014 at 11:24:15 AM by CN=Dan Rosenblatt/OU=DC/O=USEPA/C=US

APPROVED AND COMPLETED on 05/08/2014 at 06:48:06 AM by CN=Marty Monell/OU=DC/O=USEPA/C=US

Shah, Pv

From: Head, Ted <Ted.Head@ecolab.com>
Sent: Tuesday, May 06, 2014 12:52 PM
To: Shah, Pv
Subject: RE: sodium bisufate

Pv:
I'm fine with a new PRIA date of 5/30/14.

Regards,

Ted Head
Director, Global Innovative Product Registration
Law & Regulatory Affairs

ECOLAB 655 LONE OAK DRIVE, EAGAN, MN 55121
T 651 795 5770 **F** 651 204 7507 **M** 715 808 9834 **E** ted.head@ecolab.com

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From: Shah, Pv [mailto:Shah.Pv@epa.gov]
Sent: Tuesday, May 06, 2014 10:59 AM
To: Head, Ted; Carrie Daniels
Subject: sodium bisufate

Ted/Carrie
I thought PRIA due date is 5/16/2014 but it turns out that it is today. As I indicated to you we got the approval from OGC. It is already sent to FR staff for type setting. I need additional three weeks extension (just to be on safe side 5/30/2014). Could please let me know today that you are agreeing to this negotiated date?
Thanks
PV

P. V. Shah, Ph.D
Chief, Inert Ingredient Assessment Branch
Registration Division
Office of Pesticides Programs, US EPA
1200 Pennsylvania Ave., NW
Washington, DC 20460 (USA)
Phone: 703-308-1846
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For FED EX and UPS Deliveries: One Potomac Yard (South Building), 2777 Crystal Drive (Room S-7751), Arlington, VA 22202

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

April 18, 2014

MEMORANDUM

SUBJECT: PC Code: 873201, Sodium Bisulfate; Human Health Risk Assessment and Ecological Effects Assessment to Support Proposed Exemption from the Requirement of a Tolerance When Used as Inert Ingredients in Pesticide Formulations.

All PC Code: 873201
Decision No.: N/A

Petition No: IN-10526
Inert Tracking No: N/A

DP Barcode: N/A
Regulatory Action: Inert Tolerance Exemption; 40 CFR 180.940(a)
All CAS Reg. No.: 7681-38-1

FROM: David Lieu, Chemist
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505P)

5/14/2014

THROUGH: Kerry Leifer, Team Leader
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505P)

TO: PV Shah, Branch Chief
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505P)

Table of Contents

EXECUTIVE SUMMARY

Exponent on behalf of Ecolab, Inc. (370 N. Wabasha Street, St. Paul, MN 55102) is requesting that EPA expand the current sodium bisulfate tolerance exemption. Sodium bisulfate also referred to as sodium acid sulfate (CAS Reg. No. 7681-38-1) has an existing inert ingredient tolerance exemption listed in 40 CFR 180.920 for pre-harvest use. Ecolab requested that EPA expand the tolerance exemption to include use as an inert ingredient in antimicrobial formulations in accordance with 40 CFR 180.940(a), which includes use on food contact surfaces in public eating places, dairy processing equipment, and food processing equipment and utensils at no more than 2000 ppm in formulation.

Sodium bisulfate has a long history of use in pesticides as an antimicrobial disinfectant active ingredient, in pre-harvest pesticide formulations as an inert ingredient and in food applications as a food additive, pH control, and a leavening agent in cake mixes. All of these uses involve direct exposure and ingestion by humans. EPA re-registered sodium bisulfate for indoor antimicrobial residential use as a toilet bowl cleaner to control household and odor causing bacteria, *Staphylococcus spp.* (EPA, 1993). In 1993, sodium bisulfate was granted a exemption from the requirement of a tolerance when used as an acidifying/buffering agent in pesticide formulations to growing crops in accordance with 40 CFR 180.1001(d), which was revised in 2004 to 40 CFR 180.920.

Sodium bisulfate when used as a general acidifier or general food additive was a subject of Generally Recognized as Safe (GRAS) notification for which the Food and Drug Administration (FDA) found no objections with. The subject meets the FDA definition of a natural product (FDA 1998). The Joint FAO/WHO Expert Committee on Food Additives (JECFA) (JECFA, 2000, 2010a) has approved the use of sodium bisulfate as a food additive (an acidifier) in a broad range of beverage, confectionary, and general food uses at levels ranging from 500 to 4000 mg/kg. JECFA assigned an acceptable daily intake (ADI) of "not specified" because the parent sulfate anion is a natural constituent of food and a product of sulfur metabolism.

Sodium bisulfate readily dissociates to the bilsulfate anion and the sodium cation. Bisulfate/sulfate anion is a naturally-occurring constituent in many food substances as well as an essential component in a large number of mammalian (human) metabolic processes. The bisulfate/sulfate anion is present in all human tissue, with blood plasma sulfate concentrations of 2-3 mmol/L. Since the bisulfate anion is converted to sulfate in aqueous solution, toxicology studies for sodium sulfate are generally considered as relevant for sodium bisulfate.

The information presented in this document is summarized from the EPA Reregistration Eligibility Document, Mineral Acids dated September 1993, Joint FAO/WHO Expert Committee on Food Additives (JECFA) 2010, United Nation Envionment Programme (UNEP) SIDS Initial Assessment Report on sodium sulfate (2005), Institute of Medicine of the National Academies (2005) Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate and Food and Drug Administration (FDA) Generally Recognized as Safe (GRAS) Notice 1998 and Letter 2011.

The acute oral toxicity of sodium bisulfate is low (Toxicity category III). The acute oral LD_{50} in male rats was 2800 mg/kg. It was minimally irritating to the rabbit's skin (Toxicity category IV) and mildly irritating to the eyes (Toxicity category III). An acute inhalation study was available with sodium sulfate. Inhalation toxicity was not observed at 0.01 mg/l (the only dose tested). No dermal toxicity or dermal sanitization studies were available in the database.

Due to the data for sodium bisulfate, both human metabolic processes and toxicity data for sodium sulfate were used for the risk characterization. Both sodium bisulfate and sodium sulfate readily undergo hydrolysis and dissociate to sodium ions and sulfate ions in the body. Although there are no subchronic oral toxicity studies were available in the database for sodium bisulfate, studies are available for sodium sulfate.

No mutagenicity or genotoxicity studies were available in the database.

No carcinogenicity studies were available in the database. National Toxicology Program (NTP), International Agency for Research on Cancer (IARC), and Occupational Safety & Health Administration (OSHA) have not listed sodium bisulfate as a carcinogen. A DEREK analysis was performed on sodium bisulfate and no structural alerts were detected.

In two teratogenicity studies in mice, sodium sulfate was administered via subcutaneous injection and gavage at doses of 60 and 2800 mg/kg bw, respectively. Neither maternal nor developmental toxicity was observed $\leq$ 2800 mg/kg bw. This exceeds the limit dose of 1,000 mg/kg/day.

No immunotoxicity or neurotoxicity studies were available in the database.

Sodium bisulfate metabolism is essentially that of sodium cation and sulfate anion. When sodium bisulfate is added to food products containing water or after ingestion of sodium bisulfate it ionizes to sodium ions, hydrogen ions and sulfate ions. Following ingestion, sulfate anions are predominantly not absorbed from the gastrointestinal tract and are excreted unchanged in urine. However, the sulfate anion is normal constituent in the body, predominantly resulting from the body's metabolism of sulfur-containing food sources such as foods containing the essential amino acids cysteine and methionine. Sulfate anions are a vital component in a number of human biosynthetic pathways such as cartilage production and the formation of pancreatic digestive enzymes.

Based on the metabolism of sodium bisulfate to sulfate and sodium ions, both of which are essential components in the human metabolic processes, there is a lack of toxicological concern. Additionally, there is no indication of toxicity at the limit dose and a toxicological endpoint of concern for risk assessment purposes was not identified. Since no endpoint of concern was identified for the acute and chronic dietary exposure assessment and short and intermediate dermal and inhalation exposure, a quantitative risk assessment for sodium bisulfate is not necessary.

The Agency believes that amending the tolerance exemption to include 40 CFR § 180.940(a) will not significantly/measurably increase occupational exposure. The change in use pattern would be expanded to include food contact surfaces such as tableware, utensils, dairies and

beverage and food processing plants. In view of the regulatory history of sodium bisulfate, i.e., approved use under 40 CFR §180.920 and no new toxicological information to indicate otherwise, it is not necessary to quantitatively assess occupational exposure.

Based on the ecotoxicity data available on sodium sulfate, sodium bisulfate is not expected to be toxic to aquatic and sediment dwelling organisms. Toxicity to terrestrial plants is also expected to be low.

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf.

Taking into consideration all available information on sodium bisulfate, EPA concludes that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to sodium bisulfate when considering occupation, dietary exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information. Therefore, the establishment of an exemption from tolerance under 40 CFR 180.940(a) for residues of sodium bisulfate (CAS Reg. No. 7681-38-1) when used as a pesticide inert ingredient at no more than 2000 ppm in antimicrobial formulations on food-contact surfaces in public eating places, dairy processing equipment, food processing equipment and utensils can be considered assessed as safe under section 408(q) of the FFDCA.

I. BACKGROUND

Exponent on behalf of Ecolab, Inc. (370 N. Wabasha Street, St. Paul, MN 55102) is requesting that EPA expand the current sodium bisulfate tolerance exemption. Sodium bisulfate also referred to as sodium acid sulfate (CAS Reg. No. 7681-38-1) is already approved for inert ingredient tolerance exemption listed in 40 CFR 180.920 for pre-harvest use. Ecolab request that EPA expand it to include use as an inert ingredient at no more than 2000 ppm in antimicrobial formulations in accordance with 40 CFR 180.940(a), which includes use on food contact surfaces in public eating places, dairy processing equipment, and food processing equipment and utensils.

The information presented in this document is summarized primarily from the EPA Reregistration Eligibility Document, Mineral Acids dated September 1993, Joint FAO/WHO Expert Committee on Food Additives (JECFA) 2010, United Nation Envionment Programme (UNEP) SIDS Initial Assessment Report on sodium sulfate (2005) and Food and Drug Administration (FDA) Generally Recognized as Safe (GRAS) Notice 1998 and Letter 2011.

Sodium bisulfate has a long history of use in pesticides as an antimicrobial disinfectant active ingredient, as a pre-harvest pesticide inert formulation ingredient and in food applications as a food additive, pH control, and a leavening agent in cake mixes. All of these uses involve direct exposure and ingestion by humans. EPA re-registered sodium bisulfate for indoor antimicrobial residential use as a toilet bowl cleaner to control household and odor causing bacteria, Staphylococcus spp. (EPA, 1993). In 1993, sodium bisulfate was granted a exemption from the requirement of a tolerance when used as an acidifying/buffering agent in pesticide formulations to growing crops in accordance with 40 CFR 180.1001(d), which was revised in 2004 to 40 CFR 180.920.

USDA also cleared the use of sodium bisulfate as a cooling and retort water treatment agent to inhibit corrosion on the exteriors of canned goods. Sodium bisulfate is also used in the poultry industry and dairies, to acidify animal waste for the reduction of ammonia emission and as a browning inhibitor for granny smith apple slices while reducing microbial growth (Fan et al., 2009). Sodium bisulfate is Generally Recognized as Safe (GRAS) by FDA (1998) and meets the FDA definition of a natural product. JECFA (FECFA, 2000, 2010a) has approved the use of sodium bisulfate as a food additive (an acidifier) in a broad range of beverage, confectionary, and general food uses at levels ranging from 500 to 4000 mg/kg. JECFA assigned an ADI of "not specified" because the parent sulfate anion is a natural constituent of food and a product of sulfur metabolism.

II. INERT INGREDIENT PROFILE

A. Summary of Uses

In accordance with 40 CFR 180.920, sodium bisulfate is currently exempt from the requirement of a tolerance when used as an acidifying/buffering agent in pesticide formulations applied to growing crops. EPA has re-registered sodium bisulfate in solid and liquid (solutions), for indoor antimicrobial residential use as a toilet bowl cleaner to control household and odor causing bacteria, *Staphylococcus spp.* EPA (1993) specified the rate of

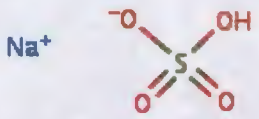
application as 30,400 ppm up to 49, 248 ppm a.i. by weight. Sodium bisulfate is used as a food additive with FDA (1998 approving sodium bisulfate as a Generally Recognized As Safe (GRAS) food additive with sulfate salts cited safe in 21 CFR 184.111; 184.1230; 184.1643; and 186.1797.

JECFA (2010b) has established an ADI for sodium bisulfate of "not specified". The term ADI "not specified" is established by JECFA to indicate a food component of very low toxicity and hazard to human health. JECFA (2010) reported that: "Sodium hydrogen sulfate [sodium bisulfate] is typically added to beverages, confectionery, fillings, syrups, processed cheeses, salad dressings, sauces, jams and jellies, and processed vegetable products at levels ranging from 500 to 4000 mg/kg for beverages. Sodium hydrogen sulfate is generally used in non-citrus-flavoured soft drinks, tea, and chocolate-flavoured and coffee-flavoured drinks, as it does not impart a sour or citric taste, as do other acidifiers."

B. Physical Chemical Properties

Some of the physical and chemical characteristics of sodium bisulfate, along with its structure and nomenclature, are found in Table 1.

Table 1. Physical and Chemical Properties of Sodium Bisulfate

Parameter	Value	Source
Structure		ChemIDplus
CAS #	7681-38-1	
Molecular Weight (g/mol)	120.06	Sigma-Aldrich MSDS
Common Names	Acid Sulfate, Sodium Pyrosulfate, Sodium Hydrogen Sulfate	Sigma-Aldrich MSDS
Physical State	Powder	Sigma-Aldrich MSDS
Melting Point (°C)	315	Chemicalbook
Boiling Point (°C) @ 19 hPa	N/A	
Density (g/cm^3 @ 20°C)	2.1	Chemicalbook
Vapor Pressure (mmHg @ 25°C)	N/A	
Partition Coefficient *(Log P)*	N/A	
Water Solubility (g/L)	120.06 g/L at 20°C (Completely soluble)	Sigma-Aldrich MSDS

pH	1.0	Sigma-Aldrich MSDS
Henry's Law Constant	N/A	EPI Suite 4.0 (registrant)

III. HUMAN HEALTH ASSESSMENT

A. Summary of Toxicity Data

Sodium bisulfate readily dissociates into the sodium cation and the bilsulfate anion. The bisulfate/sulfate anion is a naturally-occurring constituent in many food substances and a mammalian (human) metabolite therefore the existing toxicology database is limited. Since the bisulfate anion is converted to sulfate in solution, toxicology studies for sodium sulfate are generally considered as also being relevant to the toxicity of sodium bisulfate.

Acute Oral Toxicity

In an acute oral toxicity study, five Sprague-Dawley rats/sex/dose (except for 3000 mg/kg females: 10 rats), were administered by gavage, a single dose of 1750 (female only), 2000, 2250, 2500, 3000 and 3500 (male only) mg/kg of body weight of sodium bisulfate. Control rats were similarly dosed with deionized water. Surviving animals were killed after 14 days. Clinical signs (dose not specified) included weight loss, dehydration, scruffy coats, lethargy and death. Necropsy showed gross abnormalities observed in the animals that died included mottled red lungs and livers mottled with pale areas. Several of these animals were also observed to have either lesions on their stomachs or stomachs ruptured with contents emptied into the peritoneal cavity. The LD_{50} (Male) was 2800 (2393-3276) mg/kg. The study failed to establish a dose response for the females. (CAL DPR, 2002) (WHO 2010a)

Dermal Toxicity

No studies available in the database.

Inhalation Toxicity

The United Nations Environmental Programme (UNEP) in a 2005 SIDS Document on sodium sulfate references an inhalation study with an aerosol showed no adverse effects at 10 mg/m^3 or 0.01 mg/L, however the typical limit concentration testing is 2 mg/L.

Primary Eye Irritation

In a study using sodium sulfate was performed on rabbits with endpoint determination based on the DRAIZE scoring system. Sodium sulfate had no adverse effect on the iris and cornea. The substance was instilled into the conjunctival sac of the eye. The positive effects were primarily based on the conjunctvea (redness) observed in the test. The effects were reversible within 7 days. It is considered as mildly irritating to the eyes (Bayer, 1991 unpublished) (UNEP 1995).

Primary Skin Irritation

A 0.5 g portion of sodium bisulfate (moistened with deionized water) was applied to two sites, one intact and one abraded, on the back of each rabbit (sex not specified), applied

under two layer thick cotton gauze patches measuring one inch square. The entire trunks of the animals were wrapped in a non-occlusive manner for twenty-four hours. Observations showed that the intact sites had an erythema score of 1 in 3/6 rabbits at 24 hours with clearing by 72 hours. Edema score of 1 was seen in 2/6 rabbits at 24 hours and cleared by 72 hours. It is minimally irritating to the skin of rabbits.

Dermal Sensitization

No studies available in the database.

The results of the available acute toxicity studies are summarized in Table 2.

Acute Toxicity

Table 2. Acute Toxicity Profile of Sodium Bisulfate

Study Type	Results	Toxicity Category	MRIDs # /Reference
Acute Oral - rat	LD_{50} (male) = 2800 mg/kg bw LD_{50} (female) = N/A (sodium bisulfate)	III	CAL DPR 2002 WHO 2010a
Acute Dermal - N/A	N/A	N/A	N/A
Acute Inhalation - N/A	LD_{50} > 0.01 mg/L (sodium sulfate)	N/A	UNEP SIDS Sodium Sulfate 2005
Primary Eye Irritation - rabbit	Slightly irritating clearing within 7 days (sodium sulfate)	III	UNEP SIDS Sodium Sulfate 2005
Primary Skin Irritation - rabbit	Minimal irritation clearing by 72 hours (sodium bisulfate)	IV	CAL DPR 2002
Dermal Sensitization	N/A	N/A	N/A

Subchronic Toxicity -

No subchronic studies were available in the database for sodium bisulfate. However there are studies available for sodium sulfate.

According to the OECD SIDS 2005 assessment on sodium sulfate, 5 male Sprague-Dawley rats were given 0.84% of sodium sulfate in diet (320-400 mg/kg/day) for 27 and 44 weeks. There was no mortality, tumors, body weight change or significant changes in food and/or water consumption. The NOAEL was ~320-400 mg/kg/day. (Blunck & Crowther 1975) (UNEP 2005)

In 30-day oral toxicity study cited in the OECD SIDS 2005 assessment on sodium sulfate, 24 male Sprague-dawley rats were given in diet 0.0, 0.125, 0.250, 0.5, 1 and 2% sodium sulfate (estimated 125, 250, 500, 1000 and 2000 mg/kg/day) for 4 weeks. No changes in food and water consumption, body weight gain, food conversion efficiency, urine production or diarrhea. Blood hemoglobin, white blood count, serum alkaline phosphatase,

inorganic phosphate and gross organ pathology were also unaffected. The NOAEL was 2000 mg/kg/day. The LOAEL was not observed in this study (Moinuddinand Wing-Tsit Lee) (UNEP 2005)

Chronic Oral Toxicity -
No chronic studies were available in the database for sodium bisulfate.

Mutagenicity and Genotoxicity
No mutagenicity or genotoxicity studies were available in the database for sodium bisulfate. However there is one study available for sodium sulfate.
In a study cited in OECD SIDS 2005 on sodium sulfate. Sodium sulfate showed no effect in the Ames test using various strains of *S. typhimurium* (TA1535, TA1537, TA100, TA98) both with and without S9 activation in a GLP standardized test.

Carcinogenicity
No carcinogenicity studies were available in the database. National Toxicology Program (NTP), International Agency for Research on Cancer (IARC), and Occupational Safety & Health Administration (OSHA) has not listed sodium bisulfate as a carcinogen. Also a DEREK analysis was run on sodium bisulfate and no structural alerts for carcinogenicity were detected. See the Appendix for the full DEREK report.

Teratogenicity
Sodium sulfate was included in a test of a method for rapid assessment of teratogenicity. Pregnant ICR/SIM mice were given a saturated aqueous solution of sodium sulfate orally by gavage to deliver a dose of 2800 mg/kg bw per day on days 8-12 of gestation. No maternal deaths occurred and the average maternal weight gain during the treatment period was not significantly different from that of water-treated controls. Twenty-four litters were delivered alive, and none were resorbed. The mean numbers of neonates delivered alive and dead in each litter and the survival of neonates on day 3 were not statistically significantly different from those of controls. Neonatal body weights on days 1 and 3 and body-weight gain were recorded. Only body weight on day 1 was statistically significantly greater than that of controls. The maternal and developmental NOAEL = 2800 mg/kg bw, the only dose tested. The maternal and developmental LOAEL was not established (Seidenberg et al., 1986) from WHO (2000).

No reproductive studies were available in the database for sodium bisulfate.

Immunotoxicity
No immunotoxicity studies were available in the database for sodium bisulfate.

Neurotoxicity
No neurotoxicity studies were available in the database sodium bisulfate.

Metabolism and Pharmacokinetics

Sodium bisulfate mammalian metabolism is essentially that of the sodium cation and sulfate anion. As previously noted, when sodium bisulfate is added to food products containing water or after ingestion of sodium bisulfate it ionizes to sodium ions, hydrogen ions and sulfate ions.

Following ingestion, sulfate anions are predominantly not absorbed from the gastrointestinal tract and are excreted unchanged in urine. However, the sulfate anion is a normal constituent in the body, predominantly resulting from the body's metabolism of sulfur-containing food sources such as foods containing the essential amino acids cysteine and methionine. Sulfate anions are vital components in a number of human biosynthetic pathways such as cartilage production and the formation of pancreatic digestive enzymes. Additionally, the sulfate anion is also an important conjugate in the Phase II conjugation/ elimination of oxidized (OH) aromatic ring metabolites and for hydroxyl steroid hormones, such as estrogen, where it acts as a transport agent to target organ tissue receptors.

The following paragraph was taken from Institute of Medicine of the National Academies "Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate." (2005) :

> *"The nutrient is required by the body for synthesis of 3'-phosphoadenosine-5'-phosphosulfate (PAPS), which in turn is used for synthesis of many important sulfur-containing compounds such as chondroitin sulfate and cerebroside sulfate. While substantial levels of sulfate are found in foods and various sources of drinking water, the major source of inorganic sulfate for humans is from body protein turnover of the sulfur amino acids, methionine and cysteine. Dietary inorganic sulfate in food and water, together with sulfate derived from methionine and cysteine found in dietary protein, as well as the cysteine component of glutathione, provide sulfate for use in PAPS biosynthesis. Sulfate requirements are thus met when intakes include recommended levels of sulfur amino acids. For this reason, neither an Estimated Average Requirement (and thus a Recommended Dietary Allowance) nor an Adequate Intake of sulfate is established."*

Table 3. Toxicology Profile for Sodium Bisulfate

Guideline No./ Study Type	Doses Levels	MRID No. (year)/References	Results
27 and 44 week oral toxicity – rats (diet)	0.84% in diet (320-400 mg/kg/day) (sodium sulfate)	Blunch and Crowther 1975 (UNEP 2005)	NOAEL ~320-400 mg/kg/day No mortality, tumors, changes in body weight, or food/water consumption.

Table 3. Toxicology Profile for Sodium Bisulfate			
Guideline No./ Study Type	**Doses Levels**	**MRID No. (year)/References**	**Results**
4 week oral toxicity – rats (diet)	0.0, 0.01, 0.125, 0.250, 0.5, 1 and 2% (estimated 2000 mg/kg/day) (sodium sulfate)	Moinuddinand Wing-Tsit Lee (UNEP 2005)	NOAEL 2000 mg/kg/day No changes in food/water consumption, body weight gain, food conversion efficiency, urine production or diarrhea. Also no changes in blood hemoglobin, white blood count, serum alkaline phosphatase, inorganic phosphate or gross organ pathology.
Developmental Toxicity - rats	2800 mg/kg bw/day (sodium sulfate)	Seidengerb et al. 1986	Developmental NOAEL = 2800 mg/kg bw. Developmental LOAEL was not established.
Ames Test – S. typhimurium	312-5000 µg with and without activation	Bayer AG 1988 (UNEP 2005)	Negative

B. Toxicity Endpoint Selection

Sodium bisulfate readily dissociates to the bilsulfate anion and the sodium cation. Bisulfate/sulfate anion is a naturally-occurring constituent in many food substances as well as an essential component in a large number of mammalian (human) metabolic processes. The sulfate anion is a normal constituent in the body, predominantly resulting from the body's metabolism of sulfur-containing food sources such as foods containing the essential amino acids cysteine and methionine. Sulfate anions are vital components in a number of human biosynthetic pathways such as cartilage production and the formation of pancreatic digestive enzymes. Additionally, the sulfate anion is also an important conjugate in the Phase II conjugation/ elimination of oxidized (OH) aromatic ring metabolites and for hydroxyl steroid hormones. The available toxicity studies indicate that sodium bisulfate has a very low overall toxicity. A developmental toxicity study showed neither maternal nor developmental effects at 2800 mg/kg/day which is above the limit dose of 1000 mg/kg/day. Since signs of toxicity were not observed at the limit dose and sodium and bisulfate ions are present ubiquitously in the human body, an endpoint of concern for risk assessment purposes was not identified. Therefore, since no endpoint of concern was identified for the acute and chronic dietary exposure assessment and short and intermediate dermal and inhalation exposure, a quantitative risk assessment for sodium bisulfate is not necessary.

C. Special Considerations for Infants and Children

FFDCA, as amended by FQPA, directs the Agency to use an additional 10X safety factor (SF), to account for potential pre- and postnatal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. FQPA authorizes the Agency to modify the 10X FQPA SF only if reliable data demonstrate that the resulting level of exposure would be safe for infants and children.There was no hazard identified in a repeat dose rat developmental toxicity study at or above the limit dose of 1,000 mg/kg/day to either parental animals or their offspring. There is no concern for neurotoxicity, immunotoxicity or carcinogenicity for sodium bisulfate. There is no evidence to suggest susceptibility in infants and children. Since sodium and sulfate ions are found naturally in the human body as an essential component of human biosynthetic processes, endpoints to quantitatively assess dietary risk were not selected. EPA has low concentrations and no residual uncertainties with regard to pre- or postnatal toxicity from sodium bisulfate exposures. Since a qualitative assessment was conducted for potential human health exposure to copper, the 10X FQPA SF was not retained.

IV. EXPOSURE ASSESSMENT

A. Dietary Exposure:

In evaluating dietary exposure to the sodium bisulfate, EPA considered exposure under the petitioned for exemptions from the requirement of a tolerance. EPA assessed dietary exposures from sodium bisulfate in food as follows:

In conducting the dietary exposure assessment using the Dietary Exposure Evaluation Model DEEM-FCID™, Version 3.16, EPA used food consumption information from the U.S. Department of Agriculture's National Health and Nutrition Examination Survey, What We Eat In America, (NHANES/WWEIA). This dietary survey was conducted from 2003 to 2008. As to residue levels in food, no residue data were submitted for sodium bisulfate. In the absence of specific residue data, EPA has developed an approach which uses surrogate information to derive upper bound exposure estimates for the subject inert ingredient. Upper bound exposure estimates are based on the highest tolerance for a given commodity from a list of high-use insecticides, herbicides, and fungicides. A complete description of the general approach taken to assess inert ingredient risks in the absence of residue data is contained in the memorandum entitled "Alkyl Amines Polyalkoxylates (Cluster 4): Acute and Chronic Aggregate (Food and Drinking Water) Dietary Exposure and Risk Assessments for the Inerts." (D361707, S. Piper, 2/25/09) and can be found at http://www.regulations.gov in docket ID number EPA-HQ-OPP-2008-0738.

In the dietary exposure assessment, the Agency assumed that the residue level of the inert ingredient would be no higher than the highest tolerance for a given commodity. Implicit in this assumption is that there would be similar rates of degradation (if any) between the active and inert ingredient and that the concentration of inert ingredient in the scenarios

leading to these highest of tolerances would be no higher than the concentration of the active ingredient.

The Agency believes the assumptions used to estimate dietary exposures lead to an extremely conservative assessment of dietary risk due to a series of compounded conservatisms. First, assuming that the level of residue for an inert ingredient is equal to the level of residue for the active ingredient will overstate exposure. The concentration of active ingredients in agricultural products is generally at least 50 percent of the product and often can be much higher. Further, pesticide products rarely have a single inert ingredient; rather there is generally a combination of different inert ingredients used which additionally reduces the concentration of any single inert ingredient in the pesticide product in relation to that of the active ingredient.

Second, the conservatism of this methodology is compounded by EPA's decision to assume that, for each commodity, the active ingredient which will serve as a guide to the potential level of inert ingredient residues is the active ingredient with the highest tolerance level. This assumption overstates residue values because it would be highly unlikely, given the high number of inert ingredients, that a single inert ingredient or class of ingredients would be present at the level of the active ingredient in the highest tolerance for every commodity. Finally, a third compounding conservatism is EPA's assumption that all foods contain the inert ingredient at the highest tolerance level. In other words, EPA assumed 100 percent of all foods are treated with the inert ingredient at the rate and manner necessary to produce the highest residue legally possible for an active ingredient. In summary, EPA chose a very conservative method for estimating what level of inert residue could be on food, and then use this methodology to choose the highest possible residue that could be found on food and assumed that all food contained this residue. No consideration was given to potential degradation between harvest and consumption even though monitoring data shows that tolerance level residues are typically one to two orders of magnitude higher than actual residues in food when distributed in commerce.

Accordingly, although sufficient information to quantify actual residue levels in food is not available, the compounding of these conservative assumptions will lead to a significant exaggeration of actual exposures. EPA does not believe that this approach underestimates exposure in the absence of residue data.

The dietary assessment for food contact sanitizer solutions calculated the Daily Dietary Dose (DDD) and the Estimated Daily Intake (EDI). The assessment considered: application rates, residual solution or quantity of solution remaining on the treated surface without rinsing with potable water, surface area of the treated surface which comes into contact with food, pesticide migration fraction, and body weight. These assumptions are based on FDA guidelines (FDA, 2003).

FDA Food Contact Surface Sanitizing Solution Dietary Exposure Assessment Model

$$EDI\ (mg/p/day) = AR \times RS \times SA \times F \times 10^{-6} \qquad (1)$$

$$DDD\ (mg/kg/day) = AR \times RS \times SA \times F \times 10^{-6}/BW \qquad (2)$$

Where:

AR	=	Application rate (ppm)
RS	=	Residual solution (mg/cm^2)
SA	=	Surface area of the treated surface which comes into contact with food (cm^2)
F	=	Fraction of the pesticide transferred or migrated to food (unitless)
BW	=	Body weight (kg)

The input parameters listed in Table 4 below and equations 1 and 2 above are used to calculate EDI, DDD and %PAD for the three population subgroups (adult males, adult females, and infants/children).

Table 4: Input Parameters for Food Contact Surface Sanitizing Solution Dietary Exposure Assessment

Parameter	Value	Rationale
Residual Solution on Surface	1 mg/cm^2	FDA assumption
Area of Treated Surface	4,000 cm^2	FDA assumption for food utensils/surfaces
concentration in diluted solution	500 ppm	Diluted Solution concentration, based on maximum concentration (expressed in ppm).
Fraction Transferred	100%	FDA assumption
Body Weight (kg) Adult man = Adult woman = Child =	 70 60 15	EPA, 1997

EDI (mg/p/day) = AR x RS x SA x F x 10^{-6}
500 ppm * 1 mg/cm^2 * 4000 cm^2 * 100% * 10^{-6} = 20 mg/p/day

DDD (mg/kg/day) = AR x RS x SA x F x 10^{-6}/BW therefore,
for adult males 20 mg/p/day/70 kg bw/p = 0.28 mg/kg/day
for adult female 20 mg/p/day/60 kg bw/p = 0.33 mg/kg/day
for 3 year old child 20 mg/p/day/15 kg bw/p = 1.33 mg/kg/day

In estimating total dietary (food and drinking water) exposures, the exposures estimated using the FDA model for components of food contact sanitizing solutions and the estimated dietary

exposures (food and drinking water) resulting from the use of the inert ingredient in pesticide formulations are combined. The exposure estimates for the inert ingredient in pesticide formulations were derived using the Agency's DEEM-FCID model for chronic dietary exposures.

i. Acute exposure. No adverse effects attributable to a single exposure of sodium bisulfate were seen in the toxicity databases. Therefore, acute dietary exposure assessment for sodium bisulfate is not required.

ii. Chronic exposure. No adverse effects attributable to chronic exposure of sodium bisulfate were seen in the toxicity database and sodium bisulfate is a normal body constituent. Therefore, a chronic dietary exposure assessment for sodium bisulfate is not required.

iii. Cancer exposure.
The National Toxicology Program (NTP), International Agency for Research on Cancer (IARC), and Occupational Safety & Health Administration (OSHA) have not listed sodium bisulfate as a carcinogen. Sodium bisulfate is not mutagenic in the Ames test. A DEREK analysis was run on sodium bisulfate and no structural alerts for carcinogenicity were detected. Therefore, based on the lack of concern for carcinogenicity of sodium bisulfate a cancer dietary exposure assessment is not necessary to assess cancer risk.

iv. Dietary exposure from drinking water. No adverse effects attributable to acute or chronic exposure of sodium bisulfate were seen in the toxicity database and sodium bisulfate is a normal body constituent. Therefore, a dietary exposure assessment from drinking water for sodium bisulfate is not required.

B. Residential (Non-Occupational) Exposure:

i. From non-dietary exposure. The term ''residential exposure'' is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets). In the case of sodium bisulfate, the request is for use as an inert ingredient in antimicrobial formulations for use on food contact surfaces. Sodium bisulfate may also be used in products that are registered for specific uses that may result in residential exposure. However, based on the lack of toxicity, an exposure assessment from "residential exposures" was not performed.

V. AGGREGATE RISK ASSESSMENT

i. Acute Dietary Risk.
An acute aggregate risk assessment takes into account exposure estimates from acute dietary consumption of food and drinking water using the exposure assumptions discussed in section IV for acute exposure. However there was no hazard attributable to a single exposure seen in the toxicity database for sodium bisulfate; therefore there is no concern

for an acute dietary risk and an acute aggregate risk assessment was not conducted for sodium bisulfate.

ii. Chronic Dietary Risk.

A chronic aggregate risk assessment takes into account exposure estimates from chronic dietary consumption of food and drinking water using the exposure assumptions discussed in section IV from chronic exposure. However because no toxicological endpoint of concern was identified for chronic dietary exposure, there is no concern for a chronic dietary risk and a chronic aggregate risk assessment was not conducted for sodium bisulfate.

iii. Aggregate Cancer Risk for U.S. Population.

The Agency has not identified any concerns for carcinogenicity relating to sodium bisulfate; therefore, an aggregate cancer risk assessment was not conducted for sodium bisulfate.

iv. Short-term Aggregate Risk.

Short-term aggregate exposure takes into account short-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). Sodium bisulfate could be as an inert ingredient in pesticide products that could result in short-term residential exposure. However, since there are no toxicological endpoints of concern for residential exposure or food and water, EPA has concluded that the combined short-term aggregate risk assessment is not required.

v. Intermediate-Term Aggregate Risk.

Intermediate-term aggregate exposure takes into account intermediate-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). Sodium bisulfate is not expected to be used as an inert ingredient in pesticide products that could result in intermediate-term residential exposure. Since there are also no toxicological endpoints of concern for residential exposure or food and water, EPA has concluded that the combined intermediate-term aggregate risk assessment is not required.

VI. OCCUPATIONAL EXPOSURE/RISK PATHWAY

The Agency believes that amending the tolerance exemption to include 40 CFR § 180.940(a) will not significantly/measurably increase occupational exposure. The change in use pattern would be expanded to include food contact surfaces such as tableware, utensils, dairies and beverage and food processing plants. In view of the regulatory history of sodium bisulfate, i.e., approved use under 40 CFR §180.920 and no new toxicological information to indicate otherwise, it is not necessary to quantitatively assess occupational exposure.

VII. CUMULATIVE EXPSOURE

Cumulative effects from substances with a common mechanism of toxicity. Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA has not found sodium bisulfate to share a common mechanism of toxicity with any other substances, and that sodium bisulfate does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that sodium bisulfate does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's website at *http://www.epa.gov/pesticides/cumulative*.

VIII. ENVIRONMENTAL JUSTICE STATEMENT

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf.

As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, RD estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA under CSFII and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups

IX. ENVIRONMENTAL FATE CONSIDERATIONS

The environmental fate and risk information available for sodium sulfate reported by UNEP (2005) states:

"In water sodium sulfate completely dissociates into sodium and sulfate ions. The ions cannot hydrolyze. In anaerobic environments sulfate is biologically reduced to (hydrogen)

sulphide by sulfate reducing bacteria, or incorporated into living organisms as a source of sulphur, and thereby included in the sulphur cycle. Sodium sulfate is not reactive in aqueous solution at room temperature. Sodium sulfate will completely dissolve, ionize and distribute across the entire planetary "aquasphere". Some sulfates may eventually be deposited, the majority of sulfates participate in the sulphur cycle in which natural and industrial sodium sulfates are not distinguishable."

X. ECOTOXICITY

The environmental fate and risk information available for sodium sulfate reported by UNEP (2005) states:

"The BCF of sodium sulfate is very low and therefore significant bioconcentration is not expected. Sodium and sulfate ions are essential to all living organisms and their intracellular and extracellular concentrations are actively regulated. However, some plants (e.g. corn and *Kochia Scoparia*), are capable of accumulating sulfate to concentrations that are potentially toxic to ruminants. Algae were shown to be the most sensitive to sodium sulfate with an EC_{50} 120h – 1,900 g/l. For invertebrates, (*Daphnia magna*), the EC_{50} 48h = 4,580 mg/l and fish appeared to be the least sensitive with a LC_{50} 96h – 7,960 mg/l for *Pimephales promelas*. Activated sludge showed a very low sensitivity to sodium sulfate. There was no effect up to 8 g/l. Sodium sulfate is not very toxic to terrestrial plants. *Picea banksiana* was the most sensitive species, an effect was seen at 1.4 g/l. Sediment dwelling organisms were not very sensitive either, with an LC_{50} 96h = 600 mg/l for *Trycorythus sp.* Overall, it can be concluded that sodium sulfate has no acute adverse effect on aquatic and sediment dwelling organisms. Toxicity to terrestrial plants is also low."

XI. RISK CHARACTERIZATION

Sodium bisulfate metabolism is essentially that of sodium cation and sulfate anion. When sodium bisulfate is added to food products containing water or after ingestion of sodium bisulfate it ionizes to sodium ions, hydrogen ions and sulfate ions. Following ingestion, sulfate anions are predominantly not absorbed from the gastrointestinal tract and are excreted unchanged in urine. However, the sulfate anion is normal constituent in the body, predominantly resulting from the body's metabolism of sulfur containing food sources such as foods containing the essential amino acids cysteine and methionine. Sulfate anions are a vital component in a number of human biosynthetic pathways such as cartilage production and the formation of pancreatic digestive enzymes.

Since there is no indication of toxicity at the limit dose a toxicological endpoint of concern for risk assessment purposes was not identified. Since no endpoint of concern was identified for the acute and chronic dietary exposure assessment and short and intermediate dermal and inhalation exposure, a quantitative risk assessment for sodium bisulfate is not necessary.

The Agency believes that amending the tolerance exemption to include 40 CFR § 180.940(a) will not significantly/measurably increase occupational exposure. The change in use pattern would be expanded to include food contact surfaces such as tableware, utensils, dairies and beverage and food processing plants. In view of the regulatory history of sodium bisulfate, i.e., approved use under 40 CFR §180.920 and no new toxicological information to indicate otherwise, it is not necessary to quantitatively assess occupational exposure.

Taking into consideration all available information on sodium bisulfate, EPA concludes that there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure to sodium bisulfate when considering occupation, dietary exposure and all other nonoccupational sources of pesticide exposure for which there is reliable information. Therefore, the establishment of an exemption from tolerance under 40 CFR 180.940(a) for residues of sodium bisulfate (CAS Reg. No. 7681-38-1) when used as a pesticide inert ingredient at no more than 2000 ppm in antimicrobial formulations on food-contact surfaces in public eating places, dairy processing equipment, food processing equipment and utensils can be considered assessed as safe under section 408(q) of the FFDCA.

REFERENCES

Alan M. Rulis, FDA Director Office of Premarket Approval, Letter to Ms. Betty J. Pendleton Jones-Hamilton Co., dated June 5, 1998, GRAS Notice No. GRN 000003, Docket No. 98S-0104

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FDA. 2003. "Sanitizing Solutions: Chemistry Guidelines for Food Additive Petitions." http://www.cfsan.fda.gov/~dms/opa-cg3a.html. Last accessed June 9, 2003.

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Stephen Mixon, Director of Operations, Advanced Food Technologies, LLC., Letter to Antonia Mattia Office of Food Additive Safety, FDA dated October 12, 2011, "GRAS Notification for sulfuric acid and sodium sulfate blend used as an antimicrobial in meat and poultry processing."

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US EPA Registration Eligibility Document, 1993. Mineral Acids Case 6064.

World Health Organization (WHO) Food Additives Series: 44 Safety Evaluation of Certain Food Additives And Contaminants, 2000.

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APPENDIX

derek NEXUS

Derek Nexus Report

Author

HED

Report date

18 September 2013 13:27:47

Prediction date

18 September 2013 13:27:11

Program version

Derek Nexus: 3.0.1, Nexus: 1.5.0

Compound name

Structure-2

Species

bacterium, mammal

Endpoints

alpha-2-mu-Globulin nephropathy, Anaphylaxis, Bladder urothelial hyperplasia, Carcinogenicity, Cardiotoxicity, Cerebral oedema, Chloracne, Cholinesterase inhibition, Chromosome damage in vit Chromosome damage in vivo, Cumulative effect on white cell count and immunology, Cyanide-typ effects, Developmental toxicity, Genotoxicity in vitro, Genotoxicity in vivo, Hepatotoxicity, HERG channel inhibition in vitro, High acute toxicity, Irritation (of the eye), Irritation (of the gastrointestin tract), Irritation (of the respiratory tract), Irritation (of the skin), Lachrymation, Methaemoglobinaem Mutagenicity in vitro, Mutagenicity in vivo, Nephrotoxicity, Neurotoxicity, Occupational asthma, C toxicity, Oestrogenicity, Peroxisome proliferation, Phospholipidosis, Photo-induced chromosome d in vitro, Photoallergenicity, Photocarcinogenicity, Photogenotoxicity in vitro, Photogenotoxicity in Photomutagenicity in vitro, Phototoxicity, Pulmonary toxicity, Rapid prototypes: adrenal gland tox Rapid prototypes: bladder disorders, Rapid prototypes: blood in urine, Rapid prototypes: bone marr toxicity, Rapid prototypes: bradycardia, Rapid prototypes: cardiotoxicity, Rapid prototypes: chrom damage in vitro, Rapid prototypes: hepatotoxicity, Rapid prototypes: kidney disorders, Rapid proto mitochondrial dysfunction, Rapid prototypes: nephrotoxicity, Rapid prototypes: splenotoxicity, Rap prototypes: testicular toxicity, Rapid prototypes: thyroid toxicity, Respiratory sensitisation, Skin sensitisation, Teratogenicity, Testicular toxicity, Thyroid toxicity, Uncoupler of oxidative phosphor

Superendpoints

Carcinogenicity (SUPER), Chromosome damage (SUPER), Genotoxicity (SUPER), Hepatotoxicity (SUPER), HERG channel inhibition (SUPER), Irritation (SUPER), Miscellaneous endpoints (SUPE Mutagenicity (SUPER), Ocular toxicity (SUPER), Rapid prototypes: adrenal gland toxicity (SUPER) Rapid prototypes: bladder disorders (SUPER), Rapid prototypes: blood in urine (SUPER), Rapid prototypes: bone marrow toxicity (SUPER), Rapid prototypes: bradycardia (SUPER), Rapid prototy cardiotoxicity (SUPER), Rapid prototypes: chromosome damage in vitro (SUPER), Rapid prototyp hepatotoxicity (SUPER), Rapid prototypes: kidney disorders (SUPER), Rapid prototypes: mitochon dysfunction (SUPER), Rapid prototypes: nephrotoxicity (SUPER), Rapid prototypes: splenotoxicity (SUPER), Rapid prototypes: testicular toxicity (SUPER), Rapid prototypes: thyroid toxicity (SUPE

Reproductive toxicity (SUPER), Respiratory sensitisation (SUPER), Skin sensitisation (SUPER), T toxicity (SUPER)

Constraints

Perceive tautomers	true
Perceive mixtures	true
Perceive alerts without rules	false

Average molecular mass

120.06 (Lhasa Limited, version 1.0)

Exact molecular mass

119.9493 (Lhasa Limited, version 1.0)

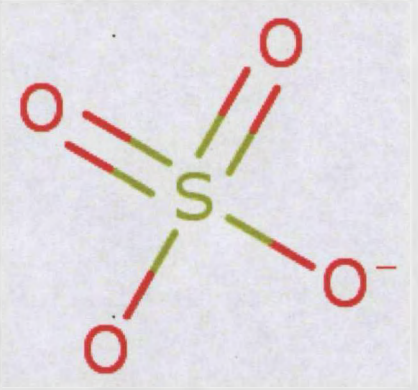
Log Kp

-4.99 (Potts & Guy, version 1.0 (LogP: BioByte Corp., version 5.3; Average Molecular Mass: Lhas Limited, version 1.0))

Log P

-2.17 (BioByte Corp., version 5.3)

Submitted compound



Structure 1 **Structure 2**

Predictions

Derek KB 2012 1.0

KnowledgeBase name

Derek KB 2012 1.0

KnowledgeBase version

1.0

KnowledgeBase last modified

29 November 2012 11:56:30

KnowledgeBase location

C:/Program Files/Lhasa Limited/Lhasa Knowledge Suite - Nexus 1.5/KnowledgeBases/org.lhasalimited.pluto.knowledge.derek_1.0.7

KnowledgeBase certified by

Lhasa Limited, Leeds, Yorkshire, UK

Nothing to report

Reasoning glossary:

Certain

Retracted

Recommendation of Division Directors
Negotiated Due Dates

Decision #:	Registration #: IN-10526	Petition #: IN-10526

☐ *See page 2 for additional registration entries*

Chemical Name: Sodium Bisulfate

Fee Category: I-002		**PRIA Decision Time Frame:** 10	
Submitted by: David	Lieu	**Branch:** OCSPP/OPP/RD	**Date:** 02/07/2014

Company: Exponent on behalf of Ecolab

Original PRIA Due Date: 10/18/2013	**Proposed New PRIA Due Date:** 05/06/2014

Previous Negotiated Due Dates: 11/29/2013

Is the "Fix" in-house? ☑ Yes ☐ No ☐ n/a **If not, date "Fix" expected:**

Negotiated Due Date Reason:

Additional Data Required	☐ Product Chemistry	☐ Toxicology	☐ Acute Tox	☐ Environmental	
	☐ Efficacy	☐ Ecological	☐ Residue	☐ Other	
Data Deficiencies	☐ Product Chemistry	☐ Acute Tox	☐ Efficacy	☐ Residue	☐ Toxicology
	☐ Environmental	☐ Ecological	☐ Labeling	☐ Other	☐ Not Submitted
Late Risk Assessment	☑ Human Health	☐ Ecological			
Interim Consideration	☐ Agency Initiated	☐ Registrant Initiated			

☐ CSF	☐ Public Process	☐ Risk Issues Environmental	☐ Risk Issues Human Health
☐ Impurities Review	☐ Label	☐ Administrative-FR Notice	☐ Other – Comment Field

Summary of Deficiency Type(s): ☐ **Not Submitted (N)** ☐ **Deficiencies (D)**

Product Chemistry: ☐ **Acute Tox:** ☐ **Efficacy:** ☐ **Labeling:** ☐ **Ecological Data:** ☐ **Other (describe):** ☑

Limited data provided by the registrants. EPA had to do reviews of literature and the effects of sequestration.

Describe Interactions with Company (describe when contacted and company's response including response to previous negotiated due dates):

US EPA initially identified potential cumulative exposure concerns for sulfites and sulfates which precluded us from being able to complete a risk assessment specific to sodium bisulfate. The issue was recently resolved and it was determined that the tolerance exemption for the specific uses can proceed forward(11/29). Then because of limited data EPA had to do literature reviews as well.

"75 Day" Letter sent? ☐ **Yes, Date sent** ☑ **No and reason for none?** *Add comments on page 2*

Rationale for Proposed Due Date: Give adequate time to prepare FR, OGC review, encoding and processing

Registrant notified that this is the last negotiation? ☐ **Yes** ☑ **Not Applicable**

Approve: ☑	**Disapprove:** ☐

If disapproved, action to be taken:

OD or DOD Signature: *CN=Marty Monell/OU=DC/O=USEPA/C=US*	**Date:** *02/10/2014*

withdrew Form

Decision #:	Registration #:	Petition #:

Issue(s) (describe in detail):

US EPA initially identified potential cumulative exposure concerns for sulfites and sulfates which precluded us from being able to complete a risk assessment specific to sodium bisulfate. The issue was recently resolved and it was determined that the tolerance exmeption for the specific uses can proceed forward. However due to the amount of time it took to resolve the concern as well as the time needed to publish a final rule in the Federal Regsiter, we will not be able to grant approval of the submission by the original PRIA due date of October 18/2013. Also US EPA was shutdown from 10/1 to 10/16. US EPA proposed a renegotaited PRIA due date of 12/18/2013 however the registrant wished to set the new due date as 11/29/2013. US EPA agreed to the registrants suggestion however the registrant was also told we do not believe this would be enough time and that it may be possible that we would have to renegotiate another due date again. Now with the limited data provided by the registrants, EPA had to do reviews of literature. Then it was determined EPA did not have enough time needed complete the risk assessment and that a renegotiation would be necessary. The new date of 05/06/2014 was agreed upon.

Comment(s):

Audit Trail for

Recommendation of Division Directors Negotiated Due Dates

PDF Name: PRIAv5.pdf
Form Number: PRIA
Document Identifier: PRIA-14038132526-DL

SUBMITTED on 02/10/2014 at 12:03:03 PM by CN=David Lieu/OU=DC/O=USEPA/C=US

APPROVED on 02/10/2014 at 12:07:27 PM by CN=Pv Shah/OU=DC/O=USEPA/C=US

APPROVED on 02/10/2014 at 01:32:09 PM by CN=Lois Rossi/OU=DC/O=USEPA/C=US

APPROVED AND COMPLETED on 02/10/2014 at 01:37:50 PM by CN=Marty Monell/OU=DC/O=USEPA/C=US

Completion of 21-Day Content Screen

PM- 8

EPA Reg. #(File Symbol) IN-10626

Decision # D_____

Data package delivered to you on 9-3-13.
(date)

Jacket/Mini-jacket will be transferred to you today.
(Pick up from Document Center)

Thank you, Kay M.

Registration Division's 21–Day Content Team

Memorandum

Date: 8 / 29 / 13

To: PM 8, Regulatory Manager

From: Information Services Branch, ITRMD

Your receipt of this data submission is not an indication that MRIDs for the enclosed studies have been posted to OPPIN.

We expect that it will be approximately 5 days from the above date before the study-level data is available in OPPIN.

If you have any questions about this process, please contact Teresa Downs (305-5363).

This is a:
- ☒ fully accepted submission
- ☐ partially accepted submission
- ☐ rejected submission

PYXIS REGULATORY CONSULTING, INC.

4110 136th St. NW
Gig Harbor, WA 98332

Phone: 253-853-7369
Fax: 253-853-5516
www.PyxisRC.com

August 20, 2013

COURIER DELIVERY

Dr. P. V. Shah
Inert Ingredient Assessment Branch/Registration Division
Office of Pesticide Programs
Document Processing Desk, 4th Floor Room S-4900
U.S. Environmental Protection Agency
2777 S. Crystal Drive
Arlington, VA 22202

RE: United Phosphorus, Inc.
Petition to Establish a Tolerance Exemption for a New Food Use Inert Ingredient
Diisopropanolamine (CAS No. 110-97-4)

Dear Dr. Shah,

On behalf of United Phosphorus, Inc. (UPI), please find enclosed a petition to establish an exemption from tolerance under 40 CFR § 180.910 for diisopropanolamine (DIPA) (CAS No. 110-97-4). DIPA is an inert ingredient currently approved for use in non-crop pesticide formulations. UPI requests establishment of an exemption from tolerance under 40 CFR § 180.910 to allow the use of DIPA as an inert ingredient (neutralizer or stabilizer) at no more than 10% in pesticide formulations applied pre- and post-harvest to crops.

In support of this petition, we submit a petition document which contains summaries of data for DIPA and in some cases, for the related chemical triisopropanolamine (TIPA) and describes the proposed use of DIPA. Summaries of new and publicly available literature data for DIPA and TIPA are provided. In support of this petition, the following documents are enclosed:

1. Three (3) copies of the Notice of Filing
2. A CD with the Notice of Filing in Word version
3. Copy of the PRIA payment submission
4. Letter of Authorization from UPI
5. Publicly available literature data summaries and tolerance exemption petition (3 copies):

49199701	Volume 1	Hauswirth, J. W. and Tillman, A. M. Diisopropanolamine Mammalian Toxicity.
49199702	Volume 2	Tillman, A. M. Diisopropanolamine: Toxicity to Non-target Organisms.
Admin	Volume 3	Tillman, A. M. and Hauswirth, J. W. Diisopropanolamine: Tolerance Exemption Petition.

UPI believes this action falls under PRIA category I001 (172; approval of a new food use inert ingredient). The PRIA fee of $18,000 has been paid. If you have any questions about this submission or need additional information, please contact me ((253) 853-7369, Ann@PyxisRC.com).

Sincerely,

Ann M. Tillman

Enclosures
cc: D. Olson, United Phosphorus, Inc.

Recommendation of Division Directors
Negotiated Due Dates

Decision #:	Registration #: IN-10526	Petition #: IN-10526

☐ *See page 2 for additional registration entries*

Chemical Name: Sodium Bisulfate

Fee Category: I-002	**PRIA Decision Time Frame:** 10	
Submitted by: David Lieu	**Branch:** OCSPP/OPP/RD	**Date:** 10/17/2013

Company: Exponent on behalf of Ecolab

Original PRIA Due Date: 10/18/2013	**Proposed New PRIA Due Date:** 11/29/2013

Previous Negotiated Due Dates:

Is the "Fix" in-house? ☑ Yes ☐ No ☐ n/a	**If not, date "Fix" expected:**

Negotiated Due Date Reason:

Additional Data Required	☐ Product Chemistry	☐ Toxicology	☐ Acute Tox	☐ Environmental	
	☐ Efficacy	☐ Ecological	☐ Residue	☐ Other	
Data Deficiencies	☐ Product Chemistry	☐ Acute Tox	☐ Efficacy	☐ Residue	☐ Toxicology
	☐ Environmental	☐ Ecological	☐ Labeling	☐ Other	☐ Not Submitted
Late Risk Assessment	☑ Human Health	☐ Ecological			
Interim Consideration	☐ Agency Initiated	☐ Registrant Initiated			

☐ CSF	☐ Public Process	☐ Risk Issues Environmental	☐ Risk Issues Human Health
☐ Impurities Review	☐ Label	☐ Administrative-FR Notice	☐ Other – Comment Field

Summary of Deficiency Type(s): ☐ **Not Submitted (N)** ☐ **Deficiencies (D)**

Product Chemistry: ☐ **Acute Tox:** ☐ **Efficacy:** ☐ **Labeling:** ☐ **Ecological Data:** ☐ **Other (describe):** ☐

Describe Interactions with Company (describe when contacted and company's response including response to previous negotiated due dates):

US EPA initially identified potential cumulative exposure concerns for sulfites and sulfates which precluded us from being able to complete a risk assessment specific to sodium bisulfate. The issue was recently resolved and it was determined that the tolerance exmeption for the specific uses can proceed forward. Asked company for extended PRIA date, 12/18/2013, but agreed to 11/29/2013.

"75 Day" Letter sent? ☐ **Yes, Date sent** ☐ **No and reason for none?** *Add comments on page 2*

Rationale for Proposed Due Date: To complete the risk assessment and proceed with final rule etc

Registrant notified that this is the last negotiation? ☐ **Yes** ☑ **Not Applicable**

Approve: ☑	**Disapprove:** ☐

If disapproved, action to be taken:

OD or DOD Signature: *CN=Marty Monell/OU=DC/O=USEPA/C=US*	**Date:** *10/25/2013*

Decision #:	Registration #:IN-10526	Petition #:IN-10526

Issue(s) (describe in detail):

US EPA initially identified potential cumulative exposure concerns for sulfites and sulfates which precluded us from being able to complete a risk assessment specific to sodium bisulfate. The issue was recently resolved and it was determined that the tolerance exmeption for the specific uses can proceed forward. However due to the amount of time it took to resolve the concern as well as the time needed to publish a final rule in the Federal Regsiter, we will not be able to grant approval of the submission by the original PRIA due date of October 18/2013. Also US EPA was shutdown from 10/1 to 10/16. US EPA proposed a renegotaited PRIA due date of 12/18/2013 however the registrant wished to set the new due date as 11/29/2013. US EPA agreed to the registrants suggestion however the registrant was also told we do not believe this would be enough time and that it may be possible that we would have to renegotiate another the due date again.

Comment(s):

Audit Trail for

Recommendation of Division Directors Negotiated Due Dates

PDF Name: PRIAv5.pdf
Form Number: PRIA
Document Identifier: PRIA-13290141045-DL

SUBMITTED on 10/23/2013 at 01:26:54 PM by CN=David Lieu/OU=DC/O=USEPA/C=US

APPROVED on 10/23/2013 at 01:52:27 PM by CN=Pv Shah/OU=DC/O=USEPA/C=US

APPROVED on 10/24/2013 at 04:21:07 PM by CN=Dan Rosenblatt/OU=DC/O=USEPA/C=US

APPROVED AND COMPLETED on 10/25/2013 at 07:05:03 AM by CN=Marty Monell/OU=DC/O=USEPA/C=US

From: Lieu, David
To: "Carrie Daniels"
Cc: Shah, Pv; Leifer, Kerry
Subject: RE: Question Regarding Inert Tolerance Petition for Sodium Bisulfate
Date: Thursday, October 17, 2013 1:50:00 PM

Hi Carrie,

I just spoke with PV regarding the matter. We will agree to the November 29th deadline that you have asked for below, however we do not believe this gives us an adequate amount of time to get a Final Rule published. Just be aware if this is the case we will have to renegotiate the PRIA due date again.

Thank you again for your time,
David L.

From: Carrie Daniels [mailto:cdaniels@exponent.com]
Sent: Thursday, October 17, 2013 1:38 PM
To: Lieu, David
Cc: Shah, Pv; Leifer, Kerry
Subject: RE: Question Regarding Inert Tolerance Petition for Sodium Bisulfate

Hi David,

While I understand the issues that went into the Sodium Bisulfate review, I would like to see if we can agree to a date that is earlier than December 18th. Would it be possible to extend it to November 29th?

Please call me if you would like to discuss this.

Regards,
Carrie

From: Lieu, David [mailto:lieu.david@epa.gov]
Sent: Thursday, October 17, 2013 1:25 PM
To: Carrie Daniels
Cc: Shah, Pv; Leifer, Kerry
Subject: RE: Question Regarding Inert Tolerance Petition for Sodium Bisulfate

Hi Carrie,

We never received a response from you regarding the email that was previously sent to you below. It was sent on September 19th. Due to the government shutdown we have not been able to follow up until today. The current PRIA due date is set for tomorrow, October 18th and we would like to renegotiate a PRIA due date for December 18, 2013 as stated below. If you agree with the renegotiated PRIA due date please provide your agreement to us in writing (email is also acceptable).

If you have any questions please let us know.

Thank you for your time,
David I.

From: Lieu, David
Sent: Thursday, September 19, 2013 2:55 PM
To: 'cdaniels@exponent.com'
Cc: Shah, Pv; Leifer, Kerry
Subject: Question Regarding Inert Tolerance Petition for Sodium Bisulfate

Hi Carrie,

I wanted to provide you with some information regarding the status of your submission for approval of a food use inert ingredient (IN # 10526). In the course of evaluating this submission, the Agency identified some potential cumulative exposure concerns for sulfites and sulfates which precluded us from being able to complete a risk assessment specific to sodium bisulfate. That issue was recently resolved a few weeks ago and it was determined that the tolerance exemption for sodium sulfate for the specific uses you are requesting can proceed forward. We are not at the point where our risk assessment is basically complete and we are in the final rounds of peer review, however, due to the amount of time it took to resolve the concern as well as the time needed to publish a final rule in the Federal Register, we will not be able to grant approval of the submission until December. Therefore we would propose a renegotiated PRIA due date of December 18, 2013. If you agree with the renegotiated PRIA due date please provide your agreement to us in writing (email is also acceptable).

If you have any questions please let us know.

Thank you for your time,
David L.

David Lieu, Chemist
Inert Ingredients Assessment Branch
Registration Division
Office of Chemical Safety and Pollution Prevention
E-mail: Lieu.David@epa.gov
Work: (703) 305-0079
Location: S-7942

derek NEXUS

Derek Nexus Report

Author

HED

Report date

18 September 2013 13:27:47

Prediction date

18 September 2013 13:27:11

Program version

Derek Nexus: 3.0.1, Nexus: 1.5.0

Compound name

Structure-2

Species

bacterium, mammal

Endpoints

alpha-2-mu-Globulin nephropathy, Anaphylaxis, Bladder urothelial hyperplasia, Carcinogenicity, Cardiotoxicity, Cerebral oedema, Chloracne, Cholinesterase inhibition, Chromosome damage in vitro, Chromosome damage in vivo, Cumulative effect on white cell count and immunology, Cyanide-type effects, Developmental toxicity, Genotoxicity in vitro, Genotoxicity in vivo, Hepatotoxicity, HERG channel inhibition in vitro, High acute toxicity, Irritation (of the eye), Irritation (of the gastrointestinal tract), Irritation (of the respiratory tract), Irritation (of the skin), Lachrymation, Methaemoglobinaemia, Mutagenicity in vitro, Mutagenicity in vivo, Nephrotoxicity, Neurotoxicity, Occupational asthma, Ocular toxicity, Oestrogenicity, Peroxisome proliferation, Phospholipidosis, Photo-induced chromosome damage in vitro, Photoallergenicity, Photocarcinogenicity, Photogenotoxicity in vitro, Photogenotoxicity in vivo, Photomutagenicity in vitro, Phototoxicity, Pulmonary toxicity, Rapid prototypes: adrenal gland toxicity, Rapid prototypes: bladder disorders, Rapid prototypes: blood in urine, Rapid prototypes: bone marrow toxicity, Rapid prototypes: bradycardia, Rapid prototypes: cardiotoxicity, Rapid prototypes: chromosome damage in vitro, Rapid prototypes: hepatotoxicity, Rapid prototypes: kidney disorders, Rapid prototypes: mitochondrial dysfunction, Rapid prototypes: nephrotoxicity, Rapid prototypes: splenotoxicity, Rapid prototypes: testicular toxicity, Rapid prototypes: thyroid toxicity, Respiratory sensitisation, Skin sensitisation, Teratogenicity, Testicular toxicity, Thyroid toxicity, Uncoupler of oxidative phosphorylation

Superendpoints

Carcinogenicity (SUPER), Chromosome damage (SUPER), Genotoxicity (SUPER), Hepatotoxicity (SUPER), HERG channel inhibition (SUPER), Irritation (SUPER), Miscellaneous endpoints (SUPER), Mutagenicity (SUPER), Ocular toxicity (SUPER), Rapid prototypes: adrenal gland toxicity (SUPER), Rapid prototypes: bladder disorders (SUPER), Rapid prototypes: blood in urine (SUPER), Rapid prototypes: bone marrow toxicity (SUPER), Rapid prototypes: bradycardia (SUPER), Rapid prototypes: cardiotoxicity (SUPER), Rapid prototypes: chromosome damage in vitro (SUPER), Rapid prototypes: hepatotoxicity (SUPER), Rapid prototypes: kidney disorders (SUPER), Rapid prototypes: mitochondrial dysfunction (SUPER), Rapid prototypes: nephrotoxicity (SUPER), Rapid prototypes: splenotoxicity (SUPER), Rapid prototypes: testicular toxicity (SUPER), Rapid prototypes: thyroid toxicity (SUPER), Reproductive toxicity (SUPER), Respiratory sensitisation (SUPER), Skin sensitisation (SUPER), Thyroid toxicity (SUPER)

Constraints

Perceive tautomers	true
Perceive mixtures	true
Perceive alerts without rules	false

Average molecular mass

120.06 (Lhasa Limited, version 1.0)

Exact molecular mass

119.9493 (Lhasa Limited, version 1.0)

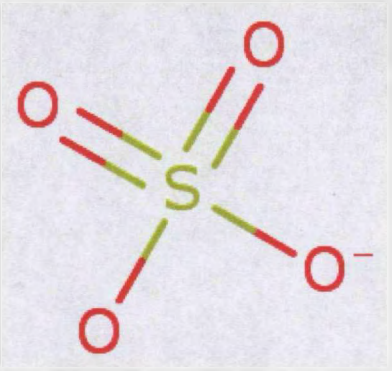
Log Kp

-4.99 (Potts & Guy, version 1.0 (LogP: BioByte Corp., version 5.3; Average Molecular Mass: Lhasa Limited, version 1.0))

Log P

-2.17 (BioByte Corp., version 5.3)

Submitted compound



Structure 1 Structure 2

Predictions

Derek KB 2012 1.0

KnowledgeBase name

Derek KB 2012 1.0

KnowledgeBase version

1.0

KnowledgeBase last modified

29 November 2012 11:56:30

KnowledgeBase location

C:/Program Files/Lhasa Limited/Lhasa Knowledge Suite - Nexus 1.5/KnowledgeBases/org.lhasalimited.pluto.knowledge.derek_1.0.7

KnowledgeBase certified by

Lhasa Limited, Leeds, Yorkshire, UK

Nothing to report

Reasoning glossary:

Certain

There is proof that the proposition is true.

Probable

There is at least one strong argument that the proposition is true and there are no arguments against it.

Plausible

The weight of evidence supports the proposition.

Equivocal

There is an equal weight of evidence for and against the proposition.

Doubted

The weight of evidence opposes the proposition.

Improbable

There is at least one strong argument that the proposition is false and there are no arguments that it is true.

Impossible

There is proof that the proposition is false.

Open

There is no evidence that supports or opposes the proposition.

Contradicted

There is proof that the proposition is both true and false.

USDA Economic Research Service

United States Department of Agriculture

The mission of the Economic Research Service is to inform and enhance public and private decision making on economic and policy issues related to agriculture, food, the environment, and rural development. Activities to support this mission involve a comprehensive program of economic research and analysis, including development of economic and statistical indicators, on a broad range of topics spanning the four goal areas of USDA:

Assist rural communities to create prosperity so they are self-sustaining, repopulating, and economically thriving;

Ensure our national forests and private working lands are conserved, restored, and made more resilient to climate change, while enhancing our water resources;

Help America promote agricultural production and biotechnology exports as America works to increase food security;

Ensure that all of America's children have access to safe, nutritious, and balanced meals.

The key accomplishments listed below summarize, by fiscal year, selected examples across the four goal areas of recent contributions made by ERS to deepen understanding of issues explored, highlight policy concerns revealed by prior analysis, and anticipate upcoming needs of policy and decision makers. Prior to FY 2009, the key accomplishments corresponded to the five USDA goal areas identified in the previous USDA Strategic Plan for FY 2000-2008.

Key Accomplishments, 2011

Key Accomplishments, 2010

Key Accomplishments, 2009

Previous Key Accomplishments

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

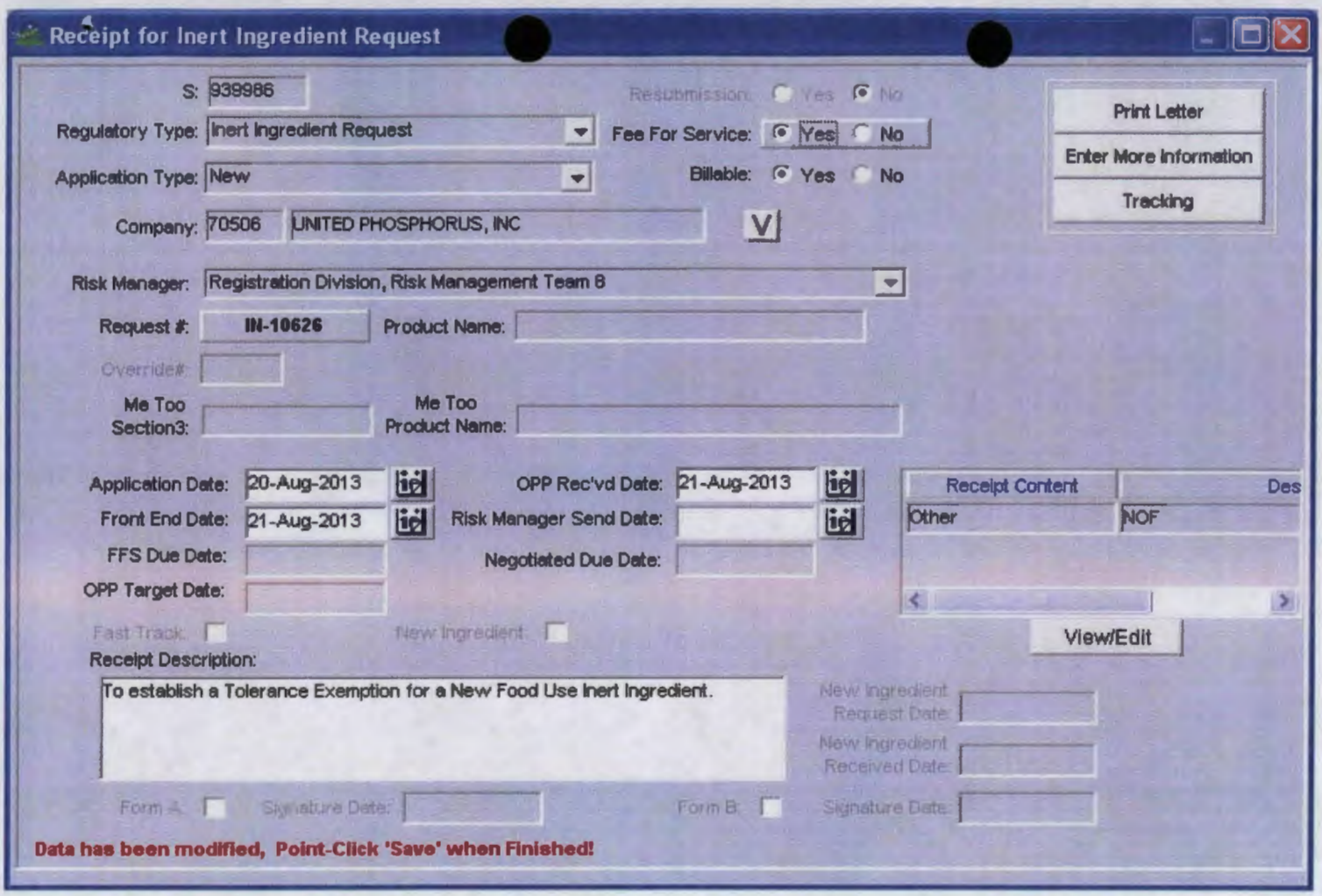
August 28, 2013

UNITED PHOSPHORUS, INC
630 FREEDOM BUSINESS CENTER, SUITE 402
KING OF PRUSSIA, PA 19406

Report of Analysis for Compliance with PR Notice 11-03

Thank you for your submittal of 21-AUG-13. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 11-03. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.


Receipt for Inert Ingredient Request
S: 939986
Resubmission: Yes No
Regulatory Type: Inert Ingredient Request
Fee For Service: Yes No
Application Type: New
Billable: Yes No
Company: 70506 UNITED PHOSPHORUS, INC
Print Letter
Enter More Information
Tracking
Risk Manager: Registration Division, Risk Management Team 8
Request #: IN-10626
Product Name:
Override#:
Me Too Section3:
Me Too Product Name:
Application Date: 20-Aug-2013
OPP Rec'vd Date: 21-Aug-2013
Front End Date: 21-Aug-2013
Risk Manager Send Date:
FFS Due Date:
Negotiated Due Date:
OPP Target Date:
Receipt Content
Des
Other
NOF
Fast Track:
New Ingredient:
View/Edit
Receipt Description:
To establish a Tolerance Exemption for a New Food Use Inert Ingredient.
New Ingredient Request Date:
New Ingredient Received Date:
Form A:
Signature Date:
Form B:
Signature Date:
Data has been modified, Point-Click 'Save' when Finished!

PYXIS REGULATORY CONSULTING, INC.

4110 136th St. NW
Gig Harbor, WA 98332

Phone: 253-853-7369
Fax: 253-853-5516
www.PyxisRC.com

August 20, 2013

COURIER DELIVERY

Dr. P. V. Shah
Inert Ingredient Assessment Branch/Registration Division
Office of Pesticide Programs
Document Processing Desk, 4th Floor Room S-4900
U.S. Environmental Protection Agency
2777 S. Crystal Drive
Arlington, VA 22202

RE: United Phosphorus, Inc.
Petition to Establish a Tolerance Exemption for a New Food Use Inert Ingredient
Diisopropanolamine (CAS No. 110-97-4)

Dear Dr. Shah,

On behalf of United Phosphorus, Inc. (UPI), please find enclosed a petition to establish an exemption from tolerance under 40 CFR § 180.910 for diisopropanolamine (DIPA) (CAS No. 110-97-4). DIPA is an inert ingredient currently approved for use in non-crop pesticide formulations. UPI requests establishment of an exemption from tolerance under 40 CFR § 180.910 to allow the use of DIPA as an inert ingredient (neutralizer or stabilizer) at no more than 10% in pesticide formulations applied pre- and post-harvest to crops.

In support of this petition, we submit a petition document which contains summaries of data for DIPA and in some cases, for the related chemical triisopropanolamine (TIPA) and describes the proposed use of DIPA. Summaries of new and publicly available literature data for DIPA and TIPA are provided. In support of this petition, the following documents are enclosed:

1. Three (3) copies of the Notice of Filing
2. A CD with the Notice of Filing in Word version
3. Copy of the PRIA payment submission
4. Letter of Authorization from UPI
5. Publicly available literature data summaries and tolerance exemption petition (3 copies):

49199701	Volume 1	Hauswirth, J. W. and Tillman, A. M. Diisopropanolamine Mammalian Toxicity.
49199702	Volume 2	Tillman, A. M. Diisopropanolamine: Toxicity to Non-target Organisms.
Admin	Volume 3	Tillman, A. M. and Hauswirth, J. W. Diisopropanolamine: Tolerance Exemption Petition.

UPI believes this action falls under PRIA category I001 (172; approval of a new food use inert ingredient). The PRIA fee of $18,000 has been paid. If you have any questions about this submission or need additional information, please contact me ((253) 853-7369, Ann@PyxisRC.com).

Sincerely,

Ann M. Tillman

Enclosures
cc: D. Olson, United Phosphorus, Inc.

period for the proposed rule from March 31, 2013 to April 30, 2013.

By order of the Board of Governors of the Federal Reserve System, acting through the Secretary of the Board under delegated authority, February 22, 2013.

Robert deV. Frierson,

Secretary of the Board.

[FR Doc. 2013–04497 Filed 2–26–13; 8:45 am]

BILLING CODE 6210–01–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2013–0023; FRL–9380–2]

Receipt of Several Pesticide Petitions Filed for Residues of Pesticide Chemicals in or on Various Commodities

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of filing of petitions and request for comment.

SUMMARY: This document announces the Agency's receipt of several initial filings of pesticide petitions requesting the establishment or modification of regulations for residues of pesticide chemicals in or on various commodities.

DATES: Comments must be received on or before March 29, 2013.

ADDRESSES: Submit your comments, identified by the docket identification (ID) number and the pesticide petition number (PP) of interest as shown in the body of this document, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute.
- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.htm.*

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: A contact person, with telephone number and email address, is listed at the end of each pesticide petition summary. You may also reach each contact person by mail at Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

If you have any questions regarding the applicability of this action to a particular entity, consult the person listed at the end of the pesticide petition summary of interest.

B. What should I consider as I prepare my comments for EPA?

1. *Submitting CBI.* Do not submit this information to EPA through regulations.gov or email. Clearly mark the part or all of the information that you claim to be CBI. For CBI information in a disk or CD–ROM that you mail to EPA, mark the outside of the disk or CD–ROM as CBI and then identify electronically within the disk or CD–ROM the specific information that is claimed as CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

2. *Tips for preparing your comments.* When submitting comments, remember to:

i. Identify the document by docket ID number and other identifying information (subject heading, **Federal Register** date and page number).

ii. Follow directions. The Agency may ask you to respond to specific questions or organize comments by referencing a Code of Federal Regulations (CFR) part or section number.

iii. Explain why you agree or disagree; suggest alternatives and substitute language for your requested changes.

iv. Describe any assumptions and provide any technical information and/or data that you used.

v. If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced.

vi. Provide specific examples to illustrate your concerns and suggest alternatives.

vii. Explain your views as clearly as possible, avoiding the use of profanity or personal threats.

viii. Make sure to submit your comments by the comment period deadline identified.

3. *Environmental justice.* EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of any group, including minority and/or low-income populations, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical or disproportionately high and adverse human health impacts or environmental effects from exposure to the pesticides discussed in this document, compared to the general population.

II. What action is the Agency taking?

EPA is announcing its receipt of several pesticide petitions filed under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA), (21 U.S.C. 346a), requesting the establishment or modification of regulations in 40 CFR part 180 for residues of pesticide chemicals in or on various food commodities. The Agency is taking public comment on the requests before responding to the petitioners. EPA is not proposing any particular action at this time. EPA has determined that the pesticide petitions described in this document contain the data or information prescribed in FFDCA section 408(d)(2); however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the pesticide petitions. After considering the public comments, EPA intends to evaluate whether and what action may be warranted. Additional data may be needed before EPA can make a final determination on these pesticide petitions.

Pursuant to 40 CFR 180.7(f), a summary of each of the petitions that

are the subject of this document, prepared by the petitioner, is included in a docket EPA has created for each rulemaking. The docket for each of the petitions is available online at *http://www.regulations.gov.*

As specified in FFDCA section 408(d)(3), (21 U.S.C. 346a(d)(3)), EPA is publishing notice of the petitions so that the public has an opportunity to comment on the requests for the establishment or modification of regulations for residues of pesticides in or on food commodities. Further information on the petitions may be obtained through the petition's summary referenced in this unit.

New Tolerance

1. *PP 2E8126.* (EPA–HQ–OPP–2012–0980). Interregional Research Project Number 4 (IR–4), 500 College Road East, Suite 201W., Princeton, NJ 08540, requests to establish tolerances in 40 CFR part 180 for residues of the fungicide, mandipropamid, 4-chloro-N-[2-[3-methoxy-4-(2-propynyloxy)phenyl]ethyl]-alpha-(2-propynyloxy)-benzeneacetamide, in or on basil, fresh at 30 parts per million (ppm); basil, dried at 200 ppm; ginseng at 0.3 ppm; bean, succulent at 0.90 ppm; cowpea, forage at 15 ppm; vegetable, fruiting, group 8–10 at 1.0 ppm; fruit, small, vine climbing, subgroup 13–07F, except fuzzy kiwifruit at 2.0 ppm; onion, bulb, subgroup 3–07A at 0.1 ppm; and onion, green, subgroup 3–07B at 7.0 ppm. Analytical method RAM 415–01 was developed for determination of mandipropamid residues in crops. This method involves extraction of mandipropamid residues from crop samples by homogenization with acetonitrile: water (80:20 v/v). Extracts are centrifuged and aliquots diluted with water prior to being cleaned-up using polymeric solid-phase extraction cartridges. Residues of mandipropamid are quantified using high performance liquid chromatography with triple quadruple mass spectrometric detection (HPLC–MS/MS). Contact: Laura Nollen, (703) 305–7390, email address: *nollen.laura@epa.gov.*

2. *PP 2E8136.* (EPA–HQ–OPP–2013–0056). Interregional Research Project Number 4 (IR–4), requests to establish tolerances in 40 CFR part 180 for residues of the herbicide, clomazone, including its metabolites and degradates, determined by measuring only clomazone, 2-[(2-chlorophenyl)methyl]-4,4-dimethyl-3-isoxazolidinone, in or on Brassica, head and stem, subgroup 5A at 0.10 ppm; rhubarb at 0.30 ppm; pea, southern, succulent, seed at 0.05 ppm; pea, southern, dry seed at 0.05 ppm; and pea, southern, hay at 0.05 ppm. There is a practical analytical method for detecting and measuring levels of clomazone in or on raw agricultural commodities with a limit of detection that allows monitoring of food for residues at or above the levels proposed in this tolerance. Samples are analyzed using an analytical method consisting of an acid reflux, a C_{18} solid phase extraction (SPE), a Florisil SPE clean-up followed by gas chromatography (GC)-mass selective detection (MSD). Contact: Sidney Jackson, (703) 305–7610, email address: *jackson.sidney@epa.gov.*

3. *PP 3E8147.* (EPA–HQ–OPP–2012–0626). Interregional Research Project Number 4 (IR–4), requests to establish tolerances in 40 CFR part 180 for residues of the insecticide, acetamiprid, (1*E*)-*N*-[(6-chloro-3-pyridinyl)methyl]-*N'*-cyano-*N*-methylethanimidamide, including its metabolites and degradates, in or on corn, sweet, kernel plus cob with husks removed at 0.01 ppm; corn, sweet, forage at 15 ppm; and corn, sweet, stover at 30 ppm. Based upon the metabolism of acetamiprid in plants and the toxicology of the parent and metabolites, quantification of the parent acetamiprid is sufficient to determine residues of concern for enforcement purposes. As a result a method was developed that involves extraction of acetamiprid from crop matrices with a solvent followed by a decantation and filtration and finally analysis by a Liquid Chromotagraphy with tandem Mass Spectrometry (LC/MS/MS) method. Contact: Andrew Ertman, (703) 308–9367, email address: *ertman.andrew@epa.gov.*

4. *PP 2F8088.* (EPA–HQ–OPP–2013–0038). ISK Biosciences Corporation, 7470 Auburn Road, Suite A, Concord, OH 44077, requests to establish tolerances in 40 CFR part 180 for the combined residues of the insecticide, flonicamid, *N*-(cyanomethyl)-4-(trifluoromethyl)-3-pyridinecarboxamide, and its metabolites, TFNA (4-trifluoromethyl nicotinic acid), TFNA–AM (4-trifluoromethylnicotinamide), and TFNG, *N*-(4-trifluoro methylnicotinoyl)glycine, calculated as the stoichiometric equivalent of flonicamid, in or on tree, nuts, crop group 14–12 at 0.09 ppm; almond at 0.09 ppm; pecan at 0.04 ppm; and almond, hulls at 10.0 ppm. The residue analytical method for the majority of crops includes an initial extraction with acetonitrile/deionized water, followed by a liquid-liquid partition with ethyl acetate. The residue method for wheat straw is similar, except that a C_{18} solid phase extraction (SPE) is added prior to the liquid-liquid partition. The final sample solution is quantitated using LC equipped with a reverse phase column and triple quadruple mass spectrometer (MS/MS). Contact: Carmen Rodia, (703) 306–0327, email address: *rodia.carmen@epa.gov.*

5. *PP 2F8130.* (EPA–HQ–OPP–2012–0576). Arysta LifeScience North America, LLC, 15401 Weston Parkway, Suite 150, Cary, NC 27513, requests to establish a tolerance in 40 CFR part 180 for residues of the fungicide fluoxastrobin, (1*E*)-[2-[[6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinyl]oxy]phenyl](5,6-dihydro-1,4,2-dioxazin-3-yl)methanone *O*-methyloxime, and its Z isomer, (1Z)-[2-[[6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinyl]oxy]phenyl](5,6-dihydro-1,4,2-dioxazin-3-yl)methanone *O*-methyloxime, in or on wheat, grain at 0.15 ppm. Adequate analytical methodology is available for enforcement purposes. The method comprises microwave solvent extraction followed by a solid phase extraction clean up and quantification by HPLC/MS/MS. The individual detector responses for measured E- and Z-isomers is summed to give total residue. Contact: Heather Garvie, (703) 308–0034, email address: *garvie.heather@epa.gov.*

6. *PP 2F8133.* (EPA–HQ–OPP–2013–0071). BASF Corporation, 26 Davis Drive, Research Triangle Park, NC 27709, requests to establish a tolerance in 40 CFR part 180 for residues of the herbicide pendimethalin, *N*-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine, and its 3,5-dinitrobenzyl alcohol metabolite (CL202347), in or on almond, hulls at 6.0 ppm. In plants, the practical method for detecting and measuring levels of pendimethalin is aqueous organic solvent extraction, column clean up, and quantitation by GC. Contact: Erik Kraft, (703) 308–9358, email address: *kraft.erik@epa.gov.*

7. *PP 2F8135.* (EPA–HQ–OPP–2013–0051). Syngenta Crop Protection LLC., P.O. Box 18300, Greensboro, NC 27419–8300, requests to establish a tolerance in 40 CFR part 180 for residues of the fungicide propiconazole, 1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl] methyl]-1*H*-1,2,4-triazole and its metabolites determined as 2,4,-dichlorobenzoic acid and expressed as parent compound, in or on rapeseed, subgroup 20A at 0.3 ppm. The metabolism data in plants and animals suggest that analytical methods to detect either the phenyl or the triazole ring would be appropriate for the measurement of residues. However, because of the natural occurrence of

compounds that interfere with the measurement of triazoles, methods designed to detect this moiety have been proven unreliable and unacceptable. Conversely, conversion of phenyl moiety to 2,4-dichlorobenzoic acid (DCBA) has proven to be satisfactory for all agricultural products analyzed to date. Analytical methods AG–626 and AG–454A were developed for the determination of residues of propiconazole and its metabolites containing the DCBA moiety. Analytical method AG–626 has been accepted and published by EPA as the tolerance enforcement method for crops. Contact: Erin Malone, (703) 347–0253, email address: *malone.erin@epa.gov.*

8. *PP 2F8139.* (EPA–HQ–OPP–2013–0008). BASF Corporation, requests to establish a tolerance in 40 CFR part 180 for residues of the herbicide, saflufenacil, in or on crayfish at 0.01 ppm. Compliance with the tolerance levels is to be determined by measuring only saflufenacil, 2-chloro-5-[3,6-dihydro-3-methyl-2,6-dioxo-4-(trifluoromethyl)-1(2*H*)-pyrimidinyl]-4-fluoro-*N*-[[methyl(1-methylethyl)amino]sulfonyl]benzamide, in or on the commodities. Adequate enforcement methodology (LC/MS/MS) methods D0603/02 (plants) and L0073/01 (livestock) is available to enforce the tolerance expression. Contact: Bethany Benbow, (703) 347–8072, email address: *benbow.bethany@epa.gov.*

Amended Tolerance

1. *PP 2E8126.* (EPA–HQ–OPP–2012–0980). Interregional Research Project Number 4 (IR–4), requests to amend the tolerances in 40 CFR 180.637 for residues of the fungicide, mandipropamid, 4-chloro-N-[2-[3-methoxy-4-(2-propynyloxy)phenyl]ethyl]-alpha-(2-propynyloxy)-benzeneacetamide, by removing the previously established tolerances in or on grape at 1.4 ppm; onion, dry bulb at 0.05 ppm; onion, green at 4 ppm; okra at 1.0 ppm; and vegetable, fruiting, group 8 at 1.0 ppm, upon establishment of the tolerances listed under "New Tolerance" for PP 2E8126, elsewhere in this document. Contact: Laura Nollen, (703) 305–7390, email address: *nollen.laura@epa.gov.*

2. *PP 2E8136.* (EPA–HQ–OPP–2013–0056). Interregional Research Project Number 4 (IR–4), requests to amend the tolerance in 40 CFR 180.425 for residues of the herbicide, clomazone, including its metabolites and degradates, determined by measuring only clomazone, 2-[(2-chlorophenyl)methyl]-4,4-dimethyl-3-isoxazolidinone, by removing the previously established tolerance on cabbage at 0.10 ppm, upon approval of the petitioned-for tolerance on brassica, stem and head subgroup 5A listed under "New Tolerance" for PP 2E8136, elsewhere in this document. Contact: Sidney Jackson, (703) 305–7610, email address: *jackson.sidney@epa.gov.*

3. *PP 3E8147.* (EPA–HQ–OPP–2012–0626). Interregional Research Project Number 4 (IR–4), requests to amend the tolerances in 40 CFR 180.578 for residues of the insecticide acetamiprid, (1*E*)-*N*-[(6-chloro-3-pyridinyl)methyl]-*N*′-cyano-*N*-methylethanimidamide, including its metabolites and degradates, by increasing the existing tolerances in meat, meat byproducts, and milk. Tolerances for cattle, goat, horse, and sheep meat are proposed at 0.30 ppm; cattle, goat, horse, and sheep fat at 0.20 ppm; cattle, goat, horse, and sheep meat byproducts at 0.70 ppm; and milk at 0.30 ppm. Based upon the metabolism of acetamiprid in plants and the toxicology of the parent and metabolites, quantification of the parent acetamiprid is sufficient to determine residues of concern for enforcement purposes. As a result, a method was developed that involves extraction of acetamiprid from crop matrices with a solvent followed by a decantation and filtration and finally analysis by a LC/MS/MS method. Contact: Andrew Ertman, (703) 308–9367, email address: *ertman.andrew@epa.gov.*

4. *PP 2F8130.* (EPA–HQ–OPP–2012–0576). Arysta LifeScience North America, LLC, requests to revise the tolerances in 40 CFR 180.609 for residues of the fungicide, fluoxastrobin, (1*E*)-[2-[[6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinyl]oxy]phenyl](5,6-dihydro-1,4,2-dioxazin-3-yl)methanone *O*-methyloxime, and its Z isomer, (1*Z*)-[2-[[6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinyl]oxy]phenyl](5,6-dihydro-1,4,2-dioxazin-3-yl)methanone *O*-methyloxime, and its phenoxy-hydroxypyrimidine, 6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinol, increasing the milk tolerance from 0.02 ppm to 0.03 ppm; and milk, fat from 0.50 ppm to 0.75 ppm. Adequate analytical methodology is available for enforcement purposes. The method comprises microwave solvent extraction followed by a solid phase extraction clean up and quantification by HPLC/MS/MS detection. The individual detector responses for measured E- and Z-isomers is summed to give total residue. Contact: Heather Garvie, (703) 308–0034, email address: *garvie.heather@epa.gov.*

New Tolerance Exemption

PP 2E8049. (EPA–HQ–OPP–2012–0585). Pennzoil-Quaker State Company, 700 Milam Street, Houston, TX 77002 c/o Wagner Regulatory Associates, 7217 Lancaster Pike, Suite A, Hockessin, DE 19707, requests to establish an exemption from the requirement of a tolerance for residues of Distillates (Fishcher-Tropsch), heavy, C_{18}-C_{50}, branched, cyclic and linear (CAS Reg. No. 848301–69–9) under 40 CFR 180.910 when used as a pesticide inert ingredient in pesticide formulations as a solvent, diluent and dust suppressant without limitations in pesticide formulations. The petitioner believes no analytical method is needed because it is not required for the establishment of a tolerance exemption for inert ingredients. Contact: Mark Dow, (703) 305–5533, email address: *dow.mark@epa.gov.*

Amended Tolerance Exemption

1. *PP 2E8080.* (EPA–HQ–OPP–2013–0098). Toxcel, LLC, 7140 Heritage Village Plaza, Gainesville, VA 20156 on behalf of Penn A Kem, LLC, 3324 Chelsea Avenue, Memphis, TN 38108, requests to amend an exemption from the requirement of a tolerance in 40 CFR 180.1263 for residues of tetrahydrofurfuryl alcohol (THFA), (CAS Reg. No. 97–99–4), when used as a pesticide inert ingredient in the form of a solvent/co-solvent in pesticide formulations, by allowing one pre-boot herbicide application to all small cereal grains, and by extending use on canola to early bolting stage, and use on soybeans up to bloom stage. The petitioner believes no analytical method is needed because it is not required for the amendment of a tolerance exemption for inert ingredients. Contact: Janet Whitehurst, (703) 305–6129, email address: *whitehurst.janet@epa.gov.*

2. *PP IN–10541.* (EPA–HQ–OPP–2013–0093). Nichino America, Inc., 4550 New Linden Hill Road, Suite 501, Wilmington DE 19808 c/o Wagner Regulatory Associates, 7217 Lancaster Pike, Suite A, Hockessin, DE 19707, requests to amend an exemption from the requirement of a tolerance in 40 CFR 180.1130 for residues of *N*-(n-octyl)-2-pyrrolidone, (CAS Reg. No. 2687–94–7), when used as a pesticide inert ingredient to include use in pesticide formulations containing the pyraflufen ethyl active ingredient. The petitioner believes no analytical method is needed because it is not required for the amendment of a tolerance exemption for inert ingredients. Contact: David Lieu, (703) 305–0079, email address: *lieu.david@epa.gov.*

List of Subjects in 40 CFR Part 180

Environmental protection, Agricultural commodities, Feed

additives, Food additives, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: February 20, 2013.

Lois Rossi,

Director, Registration Division, Office of Pesticide Programs.

[FR Doc. 2013–04594 Filed 2–26–13; 8:45 am]

BILLING CODE 6560–50–P

DEPARTMENT OF TRANSPORTATION

Office of the Secretary

49 CFR Part 37

[Docket No. DOT–OST–2013–0014]

Notice of Retrospective Review of the Americans With Disabilities Act Regulations for Over-the-Road Bus Operators; Request for Comments

AGENCY: Office of the Secretary (OST), U.S. Department of Transportation (DOT).

ACTION: Notice.

SUMMARY: The DOT is seeking comments to help conduct a review of some of the requirements of the Americans with Disabilities Act of 1990 (ADA) implementing regulations for over-the-road bus (OTRB) operators. The DOT will review regulations specified in the **SUPPLEMENTARY INFORMATION** section. Your comments will assist DOT with making decisions to modify or retain certain requirements found in these ADA regulations.

DATES: Please send your comments by April 29, 2013.

ADDRESSES: Interested persons are invited to submit written comments to assist in our review of 49 CFR part 37 subpart H to the Office of General Counsel. Mail or hand deliver comments to the Docket Management Facility, U.S. Department of Transportation, 1200 New Jersey Avenue SE., Washington, DC 20590; submit electronically at *http://www.regulations.gov*; or fax comments to 202–366–9313. All comments should include the docket number that appears in the heading of this document. All comments received will be available for examination and copying at the above address from 9 a.m. to 5 p.m., e.t., Monday through Friday, except Federal holidays. Those desiring notification of receipt of comments must include a self-addressed, stamped postcard or may print the acknowledgment page that appears after submitting comments electronically. Anyone is able to search the electronic form of all comments in any one of our dockets by the name of the individual submitting the comment (or signing the comment, if submitted on behalf of an association, business, or labor union). You may review DOT's complete Privacy Act Statement in the **Federal Register** published on April 11, 2000 (65 FR 19477).

FOR FURTHER INFORMATION CONTACT: Jill Laptosky, Attorney–Advisor, Office of Regulation and Enforcement (C–50), U.S. Department of Transportation, 1200 New Jersey Avenue SE., Washington, DC 20590, 202–493–0308 (telephone), 202–366–9313 (fax), *jill.laptosky@dot.gov*.

SUPPLEMENTARY INFORMATION: On September 28, 1998, the U.S. Department of Transportation (DOT or the Department) issued final regulations, in response to the ADA (Pub. L. 101–336, 104 Stat. 327, 42 U.S.C. 225 and 611), which required the accessibility of new over-the-road buses (OTRBs) and accessible OTRB service. An OTRB is defined as "a bus characterized by an elevated passenger deck located over a baggage compartment." 49 CFR 37.3. The regulations require commercial OTRB operators to ensure that passengers with disabilities have access to OTRB transportation. The DOT is required by 49 CFR 37.215 to review various requirements within the ADA regulations for OTRB operators. These requirements include the following: the purchase and lease requirements of new OTRBs by operators of fixed-route systems (§ 37.183), the fleet accessibility requirements for OTRB fixed-route systems of large operators (§ 37.185), the interline service requirements (§ 37.187), the service requirement for OTRB demand-responsive systems (§ 37.189), the special provision for small mixed-service operators (§ 37.191), and the interim service requirements for fixed-route operators (§ 37.193(a)). We are not reviewing any other requirements in the ADA regulations for OTRB operators *at this time.*

As part of this review, DOT is required to consider certain factors, including the percentage of accessible OTRBs in the fleets of OTRB operators, the success of such operators at meeting the requests of passengers with disabilities for accessible OTRBs in a timely manner, ridership of OTRBs by passengers with disabilities, volume of complaints by passengers with disabilities, and the cost and service impacts of these requirements. After the review, DOT will decide whether it is appropriate to revise the part 37 ADA regulations for OTRB operators or retain the current regulations without change. The DOT will publish a notice, after the review is complete, that announces our decision and our justification.

To this end, DOT requests comments and information so the Department can better review such ADA regulations and make an informed decision on whether to initiate a rulemaking to propose revisions to any of the regulations involving OTRBs and, if so, how to develop a notice of proposed rulemaking. Specifically, comments about OTRB fleet accessibility, fulfillment of accessible OTRB service requests, and ridership and volume of complaints by passengers with disabilities, would be helpful. The DOT welcomes comments from the public, including OTRB operators and individuals with disabilities, on any aspect of this notice. The Department is particularly interested in comments from OTRB operators, both large and small, on the following:

1. *The accessibility of your OTRB fleet.* How many OTRBs do you own? Of the OTRBs that you own, how many are accessible? How many OTRBs are term-leased longer than 30 days? Of the OTRBs that are term-leased, how many are accessible? Have you been successful at meeting the requests of passengers with disabilities for accessible OTRBs in a timely manner, and what challenges continue to exist in meeting these requests?

2. *Accessibility arrangements.* If your company does not own or lease an accessible OTRB, what arrangements have you made to meet the requirements to provide accessible transportation? For example, has your company made arrangements with another company that operates an accessible OTRB to provide accessible OTRB service on behalf of your company when a 48-hour advance notice request for accessible OTRB service is received?

3. *Received requests.* Within the previous 12 months, have you received any of the following inquiries, requests, or complaints, and, if so, how many?

- Inquiries regarding whether your company owns or leases an accessible OTRB,
- Inquiries regarding whether your company can provide accessible OTRB service,
- Requests for accessible OTRB service that were received with a minimum of 48-hour advance notice and satisfied according to the requested provisions,
- Number of passengers with disabilities who have used your company's accessible OTRB service, and
- Complaints regarding denial of accessible OTRB service to an individual with a disability.

Exponent
1150 Connecticut Ave., NW
Suite 1100
Washington, DC 20036

telephone 202-772-4900
facsimile 202-772-4979
www.exponent.com

February 13, 2013

PV Shah, Ph.D.
Branch Chief
Inert Ingredient Assessment Branch
Office of Pesticide Programs
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900 One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: Petition for Exemption from the Requirement of a Tolerance for: Sodium Bisulfate (CAS RN 7681-38-1) as a Pesticide Inert Ingredient in Antimicrobial Formulations in Accordance with 40 CFR § 180.940(a)

Dear Dr. Shah:

Exponent (as agent for Ecolab, EPA Company number 1677, 370 N. Wabasha St., St. Paul, MN 55102) is responding to EPA's question regarding the use rate for the inert ingredient sodium bisulfate, which is the subject of a pending petition for an exemption from the requirement of a tolerance for the use on food contact surfaces in public eating places, dairy processing equipment and food processing equipment and utensils. ***Please note that this document contains confidential business information – not for release.***

[redacted]

Claimed confidential by submitter

Claimed confidential by submitter

[redacted]

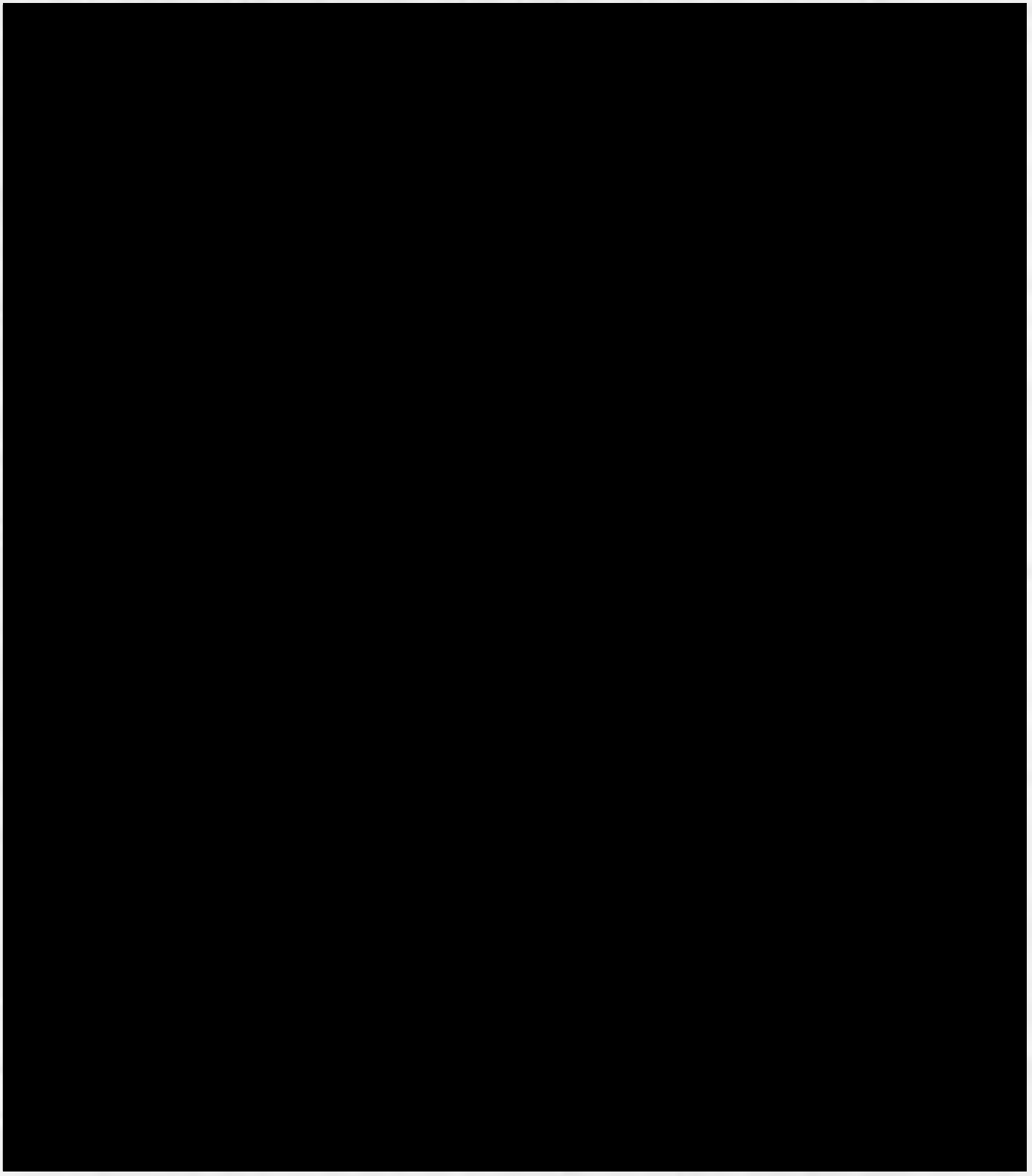
If you have questions or need further information, please contact me at 202-772-4916 or cdaniels@exponent.com.

Sincerely,

Carrie Daniels

Carrie Daniels
Senior Managing Regulatory Consultant
Exponent, Inc.

Attachment 1



Claimed confidential by submitter

Re: Fw: Ecolab's 3 reclassified inert actions

Michael Yanchulis to: Stephen Schaible 11/30/2012 08:01 AM

Cc: Elizabeth Fertich

Stephen Schaible	Fw: Ecolab's 3 reclassified inert actions	
Michael Yanchulis	*Steve, I'm confused. Receipt letters were sent out from OPPIN for thes*	

Steve,

I'm confused. Receipt letters were sent out from OPPIN for these inerts just like products. When we receive the full payment for a reclassified action, a letter from OPPIN is never generate. A letter is generated when the action is reclassified, but not when we receive the balance and that is the case for an inert, a product, etc.

Mick

Stephen Schaible	Thank, Mick! I guess we don't have an official re...	11/29/2012 05:14:58 PM

From: Stephen Schaible/DC/USEPA/US
To: Elizabeth Fertich/DC/USEPA/US@EPA
Cc: Michael Yanchulis/DC/USEPA/US@EPA
Date: 11/29/2012 05:14 PM
Subject: Fw: Ecolab's 3 reclassified inert actions

Thank, Mick! I guess we don't have an official receipt letter that goes out from OPPIN like we do with products? Given that I am in the middle of prepping for the audit, I wonder if this is a process improvement we need to make?

Beth- here is the email I received this morning on those three inert recodes.

Steve

Stephen A. Schaible, PRIA Ombudsman
Registration Division (7505P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460
ph: (703)308-9362
fax: (703)305-6920
fax: (703)305-6920

----- Forwarded by Stephen Schaible/DC/USEPA/US on 11/29/2012 05:13 PM -----

From: Michael Yanchulis/DC/USEPA/US
To: Stephen Schaible/DC/USEPA/US@EPA
Date: 11/29/2012 08:12 AM
Subject: Ecolab's 3 reclassified inert actions

Re: Recode to I002 for IN-10526, Exponent/Ecolab 180.940(a) tolerance exemption request for sodium bisulfate

Michael Yanchulis to: Stephen Schaible 11/21/2012 12:01 PM

Cc: Elizabeth Fertich, Pv Shah

Stephen Schaible	Recode to I002 for IN-10526, Exponent/Ecolab 180.940(a) tolerance exempti
Michael Yanchulis	Steve, Recoded IN-10526 to I0002. The reclassification letter is attach

Steve,

Recoded IN-10526 to I0002. The reclassification letter is attached.

Mick

Reclassification_IN10526.pdf

Stephen Schaible Mick, IIAB has identified 3 PRIA actions for whic... 11/20/2012 02:16:37 PM

From: Stephen Schaible/DC/USEPA/US
To: Michael Yanchulis/DC/USEPA/US@EPA
Cc: Elizabeth Fertich/DC/USEPA/US@EPA, Pv Shah/DC/USEPA/US@EPA
Date: 11/20/2012 02:16 PM
Subject: Recode to I002 for IN-10526, Exponent/Ecolab 180.940(a) tolerance exemption request for sodium bisulfate

Mick,

IIAB has identified 3 PRIA actions for which they believe the incorrect PRIA category was requested by the registrant and coded by the front end. Can you please recode IN-10526 from it's current PRIA category of I003 to an I002 category instead, and invoice the registrant for the outstanding balance? Please see email below for rationale.

I will be forwarding the other two recode emails shortly.

Thanks! Steve

Stephen A. Schaible, PRIA Ombudsman
Registration Division (7505P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460
ph: (703)308-9362
fax: (703)305-6920
fax: (703)305-6920

----- Forwarded by Stephen Schaible/DC/USEPA/US on 11/20/2012 02:13 PM -----

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

November 21, 2012

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

PLEASE RETURN A COPY OF THIS LETTER WITH PAYMENT
Or Pay On-Line at www.Pay.Gov (See Below for Details)

OPP Decision Number: D-471096
EPA File Symbol or Registration Number: IN-10526
Product Name: SODIUM BISULFATE
EPA Receipt Date: 19-Oct-2012
EPA Company Number: 1677
Company Name: ECOLAB INC.

RHONDA SCHULZ
ECOLAB INC.
370 NORTH WABASHA STREET
ST. PAUL, MN 55102

SUBJECT: Reclassification of Inert Petition Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your inert petition for registration that is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act. This action has been reclassified from action code I003 to action code I002:

Amend Currently Approved Inert Ingredient Tolerance or Exemption from Tolerance;New Data;

The reason for the change is that the petition includes data citations for several articles published after 1993 as references to support the new tolerance exemption under 180.940(a). These articles would be considered "new" data as they were not reviewed when the original exemption was established.

The fee for action code I002 is $5,000. We have received your payment in the amount of $3,000 towards this action. Please remit payment in the amount of $2,000 within 14 days to:

By USPS:
USEPA Washington Finance Center
Pesticide Registration Service Fee
PO Box 979074
St. Louis, MO 63197-9000

Incorrect PRIA fee paid for IN-10526, Exponent/Ecolab 180.940(a) tolerance exemption request for sodium bisulfate

Elizabeth Fertich to: Stephen Schaible 11/20/2012 12:54 PM

Cc: Pv Shah, Kerry Leifer

Elizabeth Fertich	Incorrect PRIA fee paid for IN-10526, Exponent/Ecolab 180.940(a) tolerance

Hi Steve,

We received Inert petition IN-10526 on 11/6/12. The submitter requested it be filed under PRIA category I003 (Amend currently approved inert ingredient tolerance or exemption from tolerance; no new data) and paid the appropriate fee. After reviewing the contents with PV and Kerry, it was determined that the PRIA category should be I002 (Amend currently approved inert ingredient tolerance or exemption from tolerance; new data). The original tolerance exemption for this chemical was established in 1993. The petition includes data citations for several articles published after 1993 as references to support the new tolerance exemption under 180.940(a). These articles would be considered "new" data as they were not reviewed when the original exemption was established. Let me know if you need more specific information.

Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Inert Ingredient Assessment Branch
fertich.elizabeth@epa.gov
703-347-8560

21-Day Screen Completed by Contractor

21-Day Expires on 11/9/12

Jacket # IN-10526
MRID# _____

Content Screen: Recommend to ~~Pass~~/Fail

11-3 Review: Pass/Fail/NA

Overall Status: Recommend to ~~Pass~~/Fail

Transfer This Jacket to:

Stephen Schaible

08

To the Document Center (ITRMD)

*Please transfer jacket/mini-jacket to the Product Manager Team circled below:

Minor Use Section:	**PM -5**		
Insecticide Branch:	**PM -10**	**PM-13**	
Herbicide Branch:	**PM-23**	**PM-25**	
Fungicide Branch:	**PM-20**	**PM-21**	**PM-22**
Insect/Rodent Branch:	**PM-1**	**PM-7**	

(IIAB) (PM 8)

*Reminder to PM – If applicable, pick-up data from the Screening Room.

Processed by RD's Completeness Check Team

Steve Schaible — 11/5/12

(Team Member Signature) (Date)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

October 24, 2012

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

OPP Decision Number: D-471096
EPA File Symbol or Registration Number: IN-10526
Product Name: SODIUM BISULFATE
EPA Receipt Date: 19-Oct-2012
EPA Company Number: 1677
Company Name: ECOLAB INC.

RHONDA SCHULZ
ECOLAB INC.
370 NORTH WABASHA STREET
ST. PAUL, MN 55102

SUBJECT: Receipt of Inert Petition Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your petition and certification of payment. If you submitted data with this application, the results of the PRN-2011-3 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

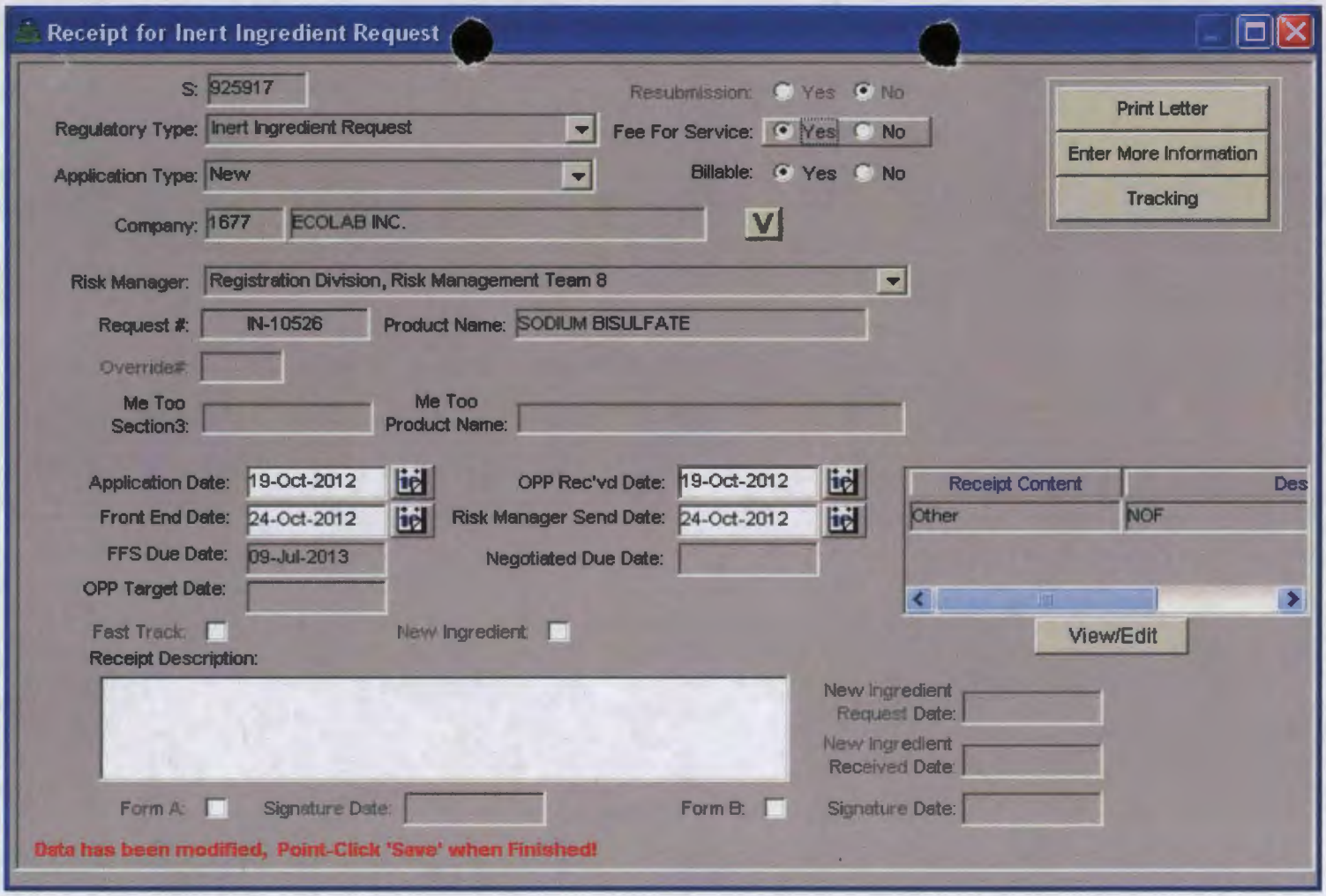
The Action has been identified as Action Code: I003

Amend Currently Approved Inert Ingredient Tolerance or Exemption from Tolerance;No New Data;

No additional payment is due at this time.

If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703)308-9362.

Sincerely,
Teresa Downs
Front End Processing Staff
Information Technology & Resources Management Division


Receipt for Inert Ingredient Request
S: 925917
Resubmission: Yes No
Regulatory Type: Inert Ingredient Request
Fee For Service: Yes No
Application Type: New
Billable: Yes No
Company: 1677 ECOLAB INC.
Print Letter
Enter More Information
Tracking
Risk Manager: Registration Division, Risk Management Team 8
Request #: IN-10526
Product Name: SODIUM BISULFATE
Override#:
Me Too Section3:
Me Too Product Name:
Application Date: 19-Oct-2012
OPP Rec'vd Date: 19-Oct-2012
Front End Date: 24-Oct-2012
Risk Manager Send Date: 24-Oct-2012
FFS Due Date: 09-Jul-2013
Negotiated Due Date:
OPP Target Date:
Receipt Content
Des
Other
NOF
Fast Track:
New Ingredient:
View/Edit
Receipt Description:
New Ingredient Request Date:
New Ingredient Received Date:
Form A:
Signature Date:
Form B:
Signature Date:
Data has been modified, Point-Click 'Save' when Finished!

Fee for Service

[redacted]

This package includes the following

- ◉ New Registration
- ○ Amendment

□ Studies? □ Fee Waiver?

□ volpay % Reduction: ___

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 8

Receipt No. S- [redacted] 925917

EPA File Symbol/Reg. No. [redacted] IN-10526

Pin-Punch Date: 10/19/2012

□ This item is NOT subject to FFS action.

Action Code:

Requested: I003

Granted: I003

Amount Due: $ 3000

Parent/Child Decisions:

▣ Inert Cleared for Intended Use ▣ Uncleared Inert in Product

Reviewer: [signature] Date: 10/23/12

Remarks:

NEW APPLICATIONS

DATE: OCT 19 2012

FILE NUMBER: ~~[illegible]~~ IN-10526

FEP (OPPIN ENTRY) LV OCT 22 2012
(Initial & date)

FILE ROOM: _____
(Initial & date)

SIG: _____
(Initial & date)

FILE ROOM: _____
(Initial & date)

✓ **ASSIGN TO PM** 8 **(NO DATA)**

____ **JACKET TO SHELF (DATA)**

SCANNED

PRIA 2 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

3/23/09

21 Day Screen Start Date: 10/19/12

Experts In-Processing Signature: ElizabethNguyen Date 11/2/12 Fee Paid: Yes ✓

Division management contacted on issues No_____Yes _____Date _____

EPA Reg. Number: 1N-10526	EPA Receipt Date: 10/19/12

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1)(link to form) signed & complete including package type					✓
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4) (Link to form)					✓
	a) All inerts (link to http://www.epa.gov/opprd001/inerts/), including fragrances, approved for the proposed uses (see Footnote A)	**yes**	**no**			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) (Link to form) completed and signed (N/A if 100% repack)					✓
	Certificate and data matrix consistent					
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	**yes**	**no**			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) (Link to form) completed and signed (N/A if source is unregistered or applicant owns the technical)					✓
5	**Data Matrix** (EPA Form 8570-35) (Link to form) both internal and external copies (PR 98-5) (Link to PR 98-5) completed and signed (N/A if 100% repack)					✓
	a) Selective Method (Fee category experts use)	**yes**	**no**			
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label** (link to http://www.epa.gov/oppfead1/labeling/lrm/) **(Electronic labels on CD are encouraged and guidance is available)(link to** http://www.epa.gov/pesticides/regulating/registering/submissions/index.htm#labels)					✓

7	**Is the data package consistent with PR Notice 86-5** (link to PRN 86-5)			X
8	**Notice of Filing (link to http://www.epa.gov/pesticides/regulating/tolerance_petitions.htm) included with petitions (link to http://www.epa.gov/pesticides/regulating/tolerances.htm)**	✓		
9	**If applicable for conventional applications, reduced risk rationale (link to http://www.epa.gov/opprd001/workplan/reducedrisk.html)**			✓
10	**Required Data (link to http://www.epa.gov/pesticides/regulating/data_requirements.htm) and/or data waivers. See Footnote C.**			
	a) List study (or studies) not included with application			

Comments:

VC
11/2/12

11-3: N/A

- no studies associated w/ inert petition

Inerts: N/A

- no CSF to review

Documents: Pass

- all required forms are present and complete

Overall status: Pass

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses. If an unapproved inert is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses **even if a product is currently registered** by consulting the inert Web

site [link to http://www.epa.gov/opprd001/inerts/lists.html] and if the inert is not approved, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch [Link to http://www.epa.gov/oppbppd1/biopesticides/contacts_bppd.htm].

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information [link to http://www.epa.gov/opprd001/inerts/tips.pdf] must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R311, R312 or R313), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

Exponent
1150 Connecticut Ave., NW
Suite 1100
Washington, DC 20036

telephone 202-772-4900
facsimile 202-772-4979
www.exponent.com

October 19, 2012

PV Shah, Ph.D.
Branch Chief
Inert Ingredient Assessment Branch
Office of Pesticide Programs
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900 One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: Petition for Exemption from the Requirement of a Tolerance for: Sodium Bisulfate (CAS RN 7681-38-1) as a Pesticide Inert Ingredient in Antimicrobial Formulations in Accordance with 40 CFR § 180.940(a)

Dear Dr. Shah:

Exponent (as agent for Ecolab, EPA Company number 1677, 370 N. Wabasha St., St. Paul, MN 55102) is submitting a petition to add an exemption from the requirement of a tolerance for the use of Sodium Bisulfate as an inert ingredient in antimicrobial formulations, for use on food contact surfaces in public eating places, dairy processing equipment and food processing equipment and utensils. The requested exemption would be listed at 40 CFR § 180.940(a). In support of this petition, please find the following enclosed:

- EPA Form 8570-1;
- Petition for Exemption from the Requirement of a Tolerance for: Sodium Bisulfate (CAS RN 7681-38-1) as a Pesticide Inert Ingredient in Antimicrobial Formulations in Accordance with 40 CFR § 180.940(a);
- Notice of Filing; and
- PRIA Category I003, Payment Confirmation Receipt.

Sodium bisulfate is ubiquitous in nature and occurs naturally in many food products. Current tolerant exemptions exist for Sodium Bisulfate at 40 CFR §180.920 (Pre-harvest). The uses as a pesticide inert ingredient under the tolerance exemption at §180.920 and as food additive have not been found to pose any unacceptable risk. The addition of the tolerance at 40 CFR §180.940(a) should not change EPA's assessment.

This submission falls under the PRIA category I003 (Amend currently approved inert ingredient tolerance or exemption from tolerance; no new data), with a review time of 8 months and a fee of $3,000.

If you have questions or need further information, please contact me at 202-772-4916 or cdaniels@exponent.com.

Sincerely,

Carrie Daniels
Senior Managing Regulatory Consultant
Exponent, Inc.

cc: Julie Spagnoli, Exponent
Ted Head, Ecolab

Please read instructions on reverse before co[illegible]ting form. Form Approved. [illegible]B No. 2070-0060. Approval expires 05-31-98

EPA United States **Environmental Protection Agency** Washington, DC 20460

☐ Registration ☐ Amendment ☒ Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
1677	PV Shah	☒ None ☐ Restricted
4. Company/Product (Name)	PM# Branch Chief	
Ecolab/Sodium Bisulfate		

5. Name and Address of Applicant *(Include ZIP Code)*
Ecolab
370 N. Wabasha St.
St. Paul, MN 55102

☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated XX-XX-XX
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☒ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Submission of a Petition for Exemption from the Requirement of a Tolerance for Sodium Bisulfate (CAS No. 7681-38-1) as an Inert Ingredient in Antimicrobial Formulations in Accordance with 40 CFR § 180.940(a).

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag
**Certification must be submitted*	If "Yes" Unit Packaging wgt. / No. per Container	If "Yes" Package wgt. / No. per Container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ Container		☐ On Bottle ☐ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☐ Other _____ ☐ Paper glued ☐ Stenciled

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Carrie Daniels	Authorized Representative	202-772-4916

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature BY:	3. Title
	Authorized Representative
4. Typed Name: Carrie Daniels	5. Date: October 19, 2012

Personal privacy information

Online Payment

Step 3: Confirm Payment 1 | 2 | 3

Thank you.
Your transaction has been successfully completed.

Pay.gov Tracking Information

Application Name: PRIA Service Fees
Pay.gov Tracking ID: 258B17RA
Agency Tracking ID: 74368196459
Transaction Date and Time: 10/17/2012 12:56 EDT

Payment Summary

Address Information

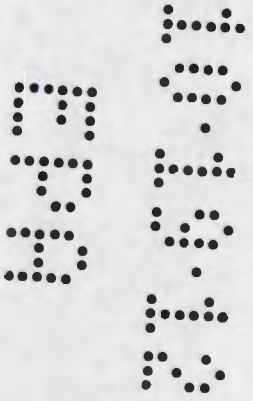
Account Holder Name: Theodore Head
Billing Address: [redacted]
Billing Address 2:
City: [redacted]
State / Province: [redacted]
Zip / Postal Code: [redacted]
Country: USA

Account Information

Card Type: Master Card
Card Number: **********4677
Decision Number:
Registration Number:
Company Name: ecolab Inc
Company Number: 1677
Action Code: I003

Payment Information

Payment Amount: $3,000.00
Transaction Date and Time: 10/17/2012 12:56 EDT



PETITION FOR EXEMPTION FROM THE REQUIREMENT OF A TOLERANCE FOR:

RESIDUES OF SODIUM BISULFATE (CAS RN 7681-38-1) AS A PESTICIDE INERT INGREDIENT IN ANTIMICROBIAL FORMULATIONS IN ACCORDANCE WITH 40 CFR §180.940(a)

SUBMITTED BY
ECOLAB, INC
370 N. WABASHA STREET
ST. PAUL, MINNESOTA 55102

PREPARED BY
EXPONENT INC
CENTER FOR CHEMICAL REGULATION AND FOOD SAFETY
1150 CONNECTICUT AVE, SUITE 1100
WASHINGTON, D.C. 20036

October 16, 2012

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I. EPA RED Mineral Acids, 1993
II. Antimicrobial Use in Meat and Poultry Processing
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VI. Sodium Bisulfate MSDS
VII. EPISuite™ 4.0 modeling Results
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INTRODUCTION

Ecolab, Inc. (Ecolab, EPA Company Number 1677, 370 N. Wabasha Street, St. Paul, MN 55102) is requesting that EPA expand the current Sodium Acid Sulfate (CAS RN 7681-38-1), also commonly referred to as Sodium Bisulfate, inert ingredient tolerance exemption listed in 40 CFR §180.920 for pre-harvest use. Ecolab request that EPA expand it to include use as an inert ingredient in antimicrobial formulations in accordance with 40 CFR §180.940(a), which includes use on food contact surfaces in public eating places, dairy processing equipment, and food processing equipment and utensils. This inert ingredient will be referred to by the more common name, and CAS nomenclature, sodium bisulfate (SBS) throughout this petition.

The information presented herein is summarized primarily from the EPA Reregistration Eligibility Document, Mineral Acids dated September 1993 (available in EPA Docket, EPA-HQ-OPP-2006-0831), Joint FAO/WHO Expert Committee on Food Additives (JECFA) and Food and Drug Administration (FDA) documents. Sodium bisulfate has a long history of safe use in pesticides as an antimicrobial disinfectant active ingredient, as a pre-harvest pesticide inert formulation ingredient and in food applications as a food additive, pH control, and a leavening agent in cake mixes. All of these uses involve direct exposure and ingestion by humans.

- EPA has re-registered sodium bisulfate for indoor antimicrobial residential use as a toilet bowl cleaner to control household and odor causing bacteria, *Staphylococcus spp.* (EPA, 1993; Refer to Appendix I).

- In accordance with 40 CFR §180.920, sodium bisulfate is exempt from the requirement of a tolerance when used as an acidifying/buffering agent in pesticide formulations to growing crops.

- USDA also cleared the use of sodium bisulfate as a cooling and retort water treatment agent to inhibit corrosion on the exteriors of canned goods. Sodium bisulfate is also used in the poultry industry and dairies, to acidify animal waste for the reduction of ammonia emission (Appendix II) and as a browning inhibitor for granny smith apple slices while reducing microbial growth (Fan et al., 2009).

- Sodium bisulfate is Generally Recognized as Safe (GRAS) by FDA (1998) and meets the FDA definition of a natural product (Appendix III).

- JECFA (JECFA, 2000, 2010a) has approved the use of sodium bisulfate as a food additive (an acidifier) in a broad range of beverage, confectionary, and general food uses at levels ranging from 500 to 4000 mg/kg. JECFA assigned an ADI of "not specified" because the parent sulfate anion is a natural constituent of food and a product of sulfur metabolism (Refer to Appendices IV and V).

Ecolab emphasizes that the data provided herein for sodium bisulfate are sufficient for EPA to conduct an FQPA regulatory review and expand the existing tolerance exemption for 40 CFR §180.920 post-harvest applications to include 40 CFR §180.940(a) antimicrobial applications without any use restrictions.

SECTION I. CHEMICAL IDENTITY

Sodium bisulfate is an acid salt that readily dissociates in aqueous solutions to generate the parent sodium cation and sulfate anion. The acidic nature is depicted by the formation of hydronium cation, H_3O^+.

$$NaHSO4 + H2O \longrightarrow Na^+ + SO4^{-2} + H_3O^+$$

Figure 1. Sodium Bisulfate Ionic Structure

$$Na^+ (HSO_4)^{-1}$$

1. Common Name:	Sodium Bisulfate
2. CAS Chemical Name:	Sulfuric Acid, Monosodium salt
3. CAS Reg Number:	7681-38-1
4. OPP Chem Code:	073201
5. Synonyms:	Sodium Acid Sulfate, Sodium Pyrosulfate, Sodium Hydrogen Sulfate
6. Chemical Formula:	$NaHSO_4$
7. Molecular Weight:	120.6

The MSDS is included as Appendix VI.

Manufacturing Processes

The following is a decription of the typical manufacturing process for sodium bisulfate.

1. Molar equivalents of sodium hydroxide and sulfuric acid are mixed to produce one mole of sodium bisulfate and water.

$$NaOH + H_2SO_4 \longrightarrow NaHSO4 + H_2O$$

2. Molar equivalents of sodium chloride salt and sulfuric acid are reacted at elevated temperatures to produce one mole of sodium bisulfate and hydrogen chloride gas.

$$NaCl + H_2SO_4 \longrightarrow NaHSO4 + HCl$$

SECTION II. PHYSICAL CHEMICAL AND ENVIRONMENTAL PROFILE

As illustrated above, sodium bisulfate is an acidic salt. EPISuite™ 4.0 calculations are generally unreliable (outside the estimation domain for the program) for inorganic salts (Appendix VII). However, the general sodium bisulfate physical chemical properties are described below.

- Non-volatile crystalline white solid
- Polar/non-lipophilic unlikely to bioaccumulate
- Freely soluble in water
- Not persistent in the environment. EPISuite™ 4.0 Primary Level Three Fugacity Model indicated a preference for the water (37.3%; half-life 360 hours) and soil (61.1%; half-life 720 hours).

SECTION III. CURRENT PESTICIDE ACTIVE INGREDIENT AND INERT INGREDIENT FORMULATION USE PATTERNS AND FOOD USE LEVELS

- In accordance with 40 CFR §180.920, sodium bisulfate is already exempt from tolerance requirements when used as an acidifying/buffering agent in pesticide formulations applied to growing crops. There are no reported restrictions.

- EPA has re-registered sodium bisulfate, in solid and liquid (solutions), for indoor antimicrobial residential use as a toilet bowl cleaner to control household and odor causing bacteria, *Staphylococcus spp*. EPA (1993) specified the rate of application as 30,400 ppm up to 49,248 ppm a.i. by weight.

- FDA (1998) has also approved sodium bisulfate as Generally Recognized as Safe (GRAS) with sulfate salts cited safe in 21 CFR §184.111; §184.1230; §184.1643; and §186.1797. There are no apparent use restrictions.

- JECFA (2010b, Appendix VIII) has established an ADI for sodium bisulfate of "not specified". The term ADI "not specified" is established by JECFA to indicate a food component of very low toxicity and hazard to human health. JECFA (2010) reports that:

> "Sodium hydrogen sulfate is typically added to beverages, confectionery, fillings, syrups, processed cheeses, salad dressings, sauces, jams and jellies, and processed vegetable products at levels ranging from 500 to 4000 mg/kg. For beverages, sodium hydrogen sulfate is generally used in non-citrus-flavoured soft drinks, tea, and chocolate-flavoured and coffee-flavoured drinks, as it does not impart a sour or citric taste, as do other acidifiers."

SECTION IV. PROPOSED USE PATTERN AND LIMITATIONS

Ecolab will use sodium bisulfate as an inert ingredient in antimicrobial pesticide formulations according to 40 CFR §180.940(a) applications, which includes use on food contact surfaces in public eating places, dairy processing equipment, and food processing equipment and utensils.

Ecolab requests that there be no limitations for the intended 40 CFR §180.940(a) use pattern.

SECTION V. POTENTIAL RESIDUES

While no specific food use residue information is available for sodium bisulfate, on the basis of the physical chemical and environmental properties analysis, as described in Section II above, significant residues and environmental persistence are not likely from the use of sodium bisulfate in antimicrobial products and rinses. Additionally, as described previously in Section III, given the widespread use of sodium bisulfate as a food additive and the fact that the parent sulfate anion is a natural constituent of food and a product of sulfur metabolism, it is not likely that the use of sodium bisulfate in 40 CFR §180.940(a) pesticide formulations will result in any potential increase in potential residues beyond those that are already approved and have current EPA tolerance exemptions.

SECTION VI. MAMMALIAN METABOLISM

Sodium bisulfate mammalian metabolism is essentially that of sodium cation and sulfate anion. As previously noted, when sodium hydrogen sulfate is added to food products containing water or after ingestion of sodium hydrogen sulfate, it ionizes to sodium ions, hydrogen ions and sulfate ions.

Excess sulfate anions, naturally-occurring components in food and a metabolite of *in vivo* sulfur oxidation, are highly water soluble and therefore eliminated in urine unchanged without the formation of toxic metabolites. Sulfate anion is also an important conjugate in the Phase II conjugation/elimination of oxidized (OH) aromatic ring metabolites and for hydroxyl steroid hormones, such as estrogen, where it acts as a transport agent to target organ tissue receptors.

The following sulfate pharmacokinetic excretion study was reported by WHO (2000):

> "The renal clearance of the sulfate ion was measured in a cross-over clinical trial in six men and two women, aged 26-35, weighing 45-98 kg, and with an estimated body surface area of 1.4-2.2 m^2. On different randomized study days at least four days apart, 1-2 h after a light breakfast (hour 0), the subjects drank either 100 ml water or a solution of 4.5 g sodium sulfate decahydrate in 100 ml water. This dose was repeated at hour 1, at which time the subjects emptied their bladders. Urine was then collected from hour 1 to hour 3, and a blood sample was taken at hour 2.
>
> The serum concentration of sulfate at hour 2 and the 2-h urinary excretion of sulfate anion were both statistically significantly increased after the sulfate dose: mean ± SD, 0.51 ± 0.05 vs 0.41 ± 0.04 mmol/L and 2.4 ± 0.87 vs 1.6 ± 0.46 mmol/L × 73 m^2 body surface area. The renal clearance of sulfate after the sulfate dose was greater than that after water, but the difference was not statistically significant. The authors also reported, with no details, that in a separate experiment, a 6-g oral dose of ascorbic acid had no effect on the

urinary excretion of endogenous inorganic sulfate over 12 h (Morris & Levy, 1983)."

SECTION VII. MAMMALIAN TOXICOLOGY PROFILE

Because bisulfate/sulfate anion is a naturally-occurring constituent in many food substances and a mammalian (human) metabolite, the existing toxicology database is limited. As noted previously, because the bisulfate anion is converted to sulfate in solution, toxicology studies for sodium sulfate are generally considered as relevant for sodium bisulfate as well.

Following is a summary of the overall toxicology profile:

- Not acutely toxic by the oral route of ingestion, 2800 mg/kg bw in male and >2500 mg/kg bw in female rats (EPA Cat III)
- Not a rabbit skin irritant (EPA Cat IV)
- Does not bioaccumulate; readily excreted
- Not Listed as a carcinogen by NTP, IARC, or OSHA

Acute Toxicity Studies

- 50263-015 182474; Acute oral toxicity; 811; Rat; Northview Pacific Laboratories, Inc. Study X8G081G; 3/15/90; Sodium Bisulfate (reported by CAL DPR, 2002, Appendix IX)

  "5/sex/dose (except for 3000 mg/kg females: 10 rats), administered by gavage; 1750 (F only), 2000, 2250, 2500, 3000 and 3500 (M only) mg/kg of body weight; mortality: 1750 (F): 1/5; 2000 (M/F): 0/5, 2/5; 2250 (M/F): 1/5; 2500 (M/F): 0/5, 4/5; 3000 (M/F): 3/5, 1/10; 3500 (M): 4/5; clinical signs (dose not specified): weight loss, dehydration, scruffy coats, lethargy and death; necropsy: gross abnormalities observed in the animals that died on test included mottled red lungs and livers mottled with pale areas; several of these animals were also observed to have either lesions on their stomachs or stomachs ruptured with contents emptied into the peritoneal cavity; LD_{50} (M) = 2800 (2393-3276) mg/kg; the study failed to establish a dose-response for the females…"

- WHO (2010a)

  Groups of male and female Sprague-Dawley rats were gavaged with sodium hydrogen sulfate at a single oral dose of 1750, 2000, 2250, 2500, 3000 or 3500 mg/ kg body weight (bw) to determine its acute oral toxicity. Fifty-five animals were treated in total. Control rats were similarly dosed with deionized water. Surviving animals were killed after 14 days. The oral median lethal dose (LD_{50}) was determined to be 2800 mg/kg bw in males and >2500 mg/kg bw in females. Fewer females than males died. As the test progressed, it was decided to stop dosing the females, as it was clear that the LD_{50} was above 2500 mg/kg bw. Effects observed during the study included weight loss, dehydration, scruffy coats, lethargy and death. Gross abnormalities observed in the

animals that died during the study included mottled red lungs, pale mottled livers and stomach lesions or ruptures (Northview Pacific Laboratories, 1990).

- 50263-015 182475; Primary Skin Irritation Study; 815; Rabbit; Northview Pacific Laboratories, Inc., NVP Report # X8G081G; 3/15/90; Sodium Bisulfate; 6 rabbits sex not specified (reported by CAL DPR, 2002).

  "A 0.5 g portion of the test material (moistened with deionized water) was applied to two sites, one intact and one abraded, on the back of each animal, applied under two layer thick cotton gauze patches measuring one inch square; the entire trunks of the animals were wrapped in a non-occlusive manner for twenty-four hours; observations (intact sites): erythema (score 1) was noted in 3/6 rabbits at 24 hours, with clearing by 72 hours; edema (score 1) was seen in 2/6 rabbits at 24 hours and cleared by 72 hours; Toxicity Category IV."

- UNEP (2005, Appendix X)

  "The acute toxicity (LD_{50}) of sodium sulfate has not been reliably established but is probably far in excess of 5000 mg/kg. In an inhalation study with an aerosol, no adverse effects were found at 10 mg/m^3. Also human data indicate a very low acute toxicity of sodium sulfate. Human clinical experience indicates that very high oral doses of sodium sulfate, 300 mg/kg bw up to 20 grams for an adult, are well tolerated, except from (intentionally) causing severe diarrhea."

Developmental Toxicity in Mice (WHO, 2000)

- "As part of a study of the teratogenicity of morphine sulfate and other pharmacological agents, groups of pregnant CF-1 albino mice were injected subcutaneously on gestation day 8 or 9 with sodium sulfate at 60 mg/kg bw given as 10 mg/ml in water. Examination of the excised fetuses revealed some statistically significant differences from saline-treated controls, but none of the measured parameters was consistently affected. Although skeletal abnormalities were observed in both groups, the difference seen from saline controls after dosing on day 9 of gestation was not significant, and the anomalies did not appear to involve fusions of the axial skeleton (Arcuri & Gautieri, 1973)."

- "Sodium sulfate was included in a test of a method for rapid assessment of teratogenicity. Pregnant ICR/SIM mice were given a saturated aqueous solution of sodium sulfate orally by gavage to deliver a dose of 2800 mg/kg bw per day on days 8-12 of gestation. No maternal deaths occurred and the average maternal weight gain during the treatment period was not significantly different from that of water-treated controls. Twenty-four litters were delivered alive, and none were resorbed. The mean numbers of neonates delivered alive and dead in each litter and the survival of neonates on day 3 were not statistically significantly different from those of controls. Neonatal body weights on days 1 and 3 and body-weight gain were recorded; only body weight on day 1 was statistically significantly greater than that of controls (Seidenberg et al., 1986)."

Other Relevant Feeding Studies

- WHO (2010a):

"Artificially reared neonatal piglets were used as a model to evaluate the effect of inorganic sulfate on bowel function in human infants.

Two experiments were conducted:

The first evaluated the effect of high levels of sulfate on growth, feed intake and consistency of feces, and the second determined the dose at which at least 50% of the pigs developed non-pathogenic diarrhea. Following a 5-day acclimatization period, 40 piglets were distributed into four groups for each experiment. Piglets were fed liquid diets only via an Autosow and did not have access to drinking-water. Inorganic sulfate was added to the diets as anhydrous sodium sulfate at levels of 0, 1200, 1600 and 2000 mg/l for experiment 1 (18-day study) and 0, 1800, 2000 and 2200 mg/l for experiment 2 (16-day study). Piglets were individually caged and weighed daily, and the volume of diet for each piglet was adjusted according to its body weight. Feed intake and consistency of feces were recorded 3 times daily. Rectal swabs were taken from those piglets with soft or liquid stools and analysed for haemolytic *Escherichia coli* and rotavirus. At the end of each experiment, piglets were sedated and killed. Urine samples were taken, and the kidneys were removed. *The levels of added sulfate did not affect the growth of the piglets or their feed intake*. Levels of 2000 and 2200 mg sulfate/l resulted in practically all (90–100%) piglets having diarrhea, beginning 2 days after the start of the trial and persisting throughout the experimental period. Rectal swabs were negative, from which the authors concluded that the piglets had non-pathogenic diarrhea. Kidney weight was not affected by added sulfate. Sulfate concentrations in the urine reached a maximum in the piglets fed diets with 1600 and 1800 mg sulfate/l in experiments 1 and 2, respectively ($P < 0.05$), but declined at higher levels.

Based on the results, the authors concluded that the concentration of added sulfate at which 50% of piglets develop non-pathogenic diarrhea is between 1600 and 1800 mg/l (Gomez et al., 1995)."

- Observations in humans (infants and adults)

"In 1999, the United States Environmental Protection Agency and Centers for Disease Control and Prevention conducted a study on the health effects from exposure to high levels of sulfate in the drinking-water in two sensitive populations (infants and transient adults). For the infant study, the authors intended to conduct a prospective cohort study of newborn infants whose mothers planned to feed their infants formula mixed with tap water. However, a pilot study involving a self-administered questionnaire to all women attending 32 clinics to determine how many women planned to use tap water to mix infant formula for their babies revealed that very few infants were exposed to tap water containing high levels of sulfate. One hundred and five adult volunteers were randomly assigned to one of five sulfate groups: 0 mg/l ($n = 24$), 250 mg/l ($n = 10$), 500 mg/l ($n =$

10), 800 mg/l (n = 33) or 1200 mg/l (n = 28). Bottled water was provided for the volunteers for 6 days. The bottled water for days 1, 2 and 6 was unsupplemented, whereas the bottles for days 3–5 contained water with added sulfate. Bottles were returned to estimate how much water was consumed each day. Volunteers recorded the number of bowel movements each day. There were no statistically significant differences in the bowel movements among the groups on days 3–6, nor were there any statistically significant differences in the bowel movements when comparing days 1 and 2 with days 3–5, within each dose group.

The authors concluded that there was no statistically significant increase in reports of diarrhea with increasing dose of sulfate in the drinking-water (United States Environmental Protection Agency, 1999)."

Genotoxicity and Carcinogenicity

There are no reported genotoxicity studies for sodium bisulfate and it is not listed as a carcinogen by NTP, IARC, or OSHA.

The UNEP (2005, Appendix X) SIDs for Sodium Sulfate reported negative AMES results. Additionally, UNEP reported that a non-GLP chronic feeding study (1975) in which male Sprague-Dawley rats were fed 0.84% sodium sulfate in the diet for up to 27 and 44 weeks as the control in a toxicity study for Azo Dyes did not result in mortality or the formation of tumors. Moreover, there were no significant differences in overall body weight gain or in liver weight.

Endocrine Disruptor Effects

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and inert ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system.

EPA did not report having any available information to suggest that sodium bisulfate would have any endocrine effects. When the appropriate screening and/or testing protocols under the EDSP have been developed, sodium bisulfate may be subject to additional screening and/or testing to better characterize effects related to endocrine disruption. This does not impact the current regulatory status of sodium bisulfate.

SECTION VIII. SAFETY ASSESSMENT

A. Acute and Chronic Reference Doses

In the Reregistration Eligibility Decision Document for Mineral Acids (1993), EPA stated:

> "The four mineral acids [which included sodium bisulfate] pose no human dietary risks. People may be exposed to these chemicals when they are used as antimicrobials, however this exposure involves such dilute solutions that it is believed to be inconsequential."

JECFA conducts its risk assessment for ionizable salts based on the constituent cation and anions, for SBS Na^{+} and HSO_4^{-1} both of which are found ubiquitous in nature and many food products and also result from human metabolism. JECFA (2000) has established an ADI for sodium bisulfate of "not specified". The term ADI "not specified" is established by JECFA to indicate:

> "....a food component of very low toxicity which, on the basis of the available chemical, biological, toxicological, and other data, the total dietary intake of the substance arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food, does not, in the opinion of the Committee, represent a hazard to health...the establishment of an ADI expressed in numerical form is deemed unnecessary."

Additionally, on the basis of the data summarized in Section VII, no acute or chronic toxicity endpoints have been established for acute and or chronic dietary risk assessments. Therefore no acute or chronic exposure assessments are warranted.

B. Special Consideration for Infants and Children and Rationale that the FQPA Safety Factor is not Required

The FQPA Safety Factor (as required by the Food Quality Protection Act of 1996) is intended to provide an additional 10-fold safety factor (10X), to protect for special sensitivity in infants and children to specific pesticide residues in food, drinking water, or residential exposures, or to compensate for an incomplete database. EPA concluded there are no endpoints of concern for oral, dermal, or inhalation exposure to sodium bisulfate based on the low toxicity observed in studies conducted near or above testing limit doses as established in the OPPTS 870 series harmonized test guidelines.

C. Population Adjusted Dose (PAD)

The Population Adjusted Dose (PAD) is not relevant since it is derived from an ADI, aRfD or cRfD and none were assigned for sodium bisulfate.

D. Aggregate Exposure and Risk

1. Potential Dietary and Residential Exposures

As previously noted in Sections III and IV, sodium bisulfate (and its hydrolyzed congener sodium sulfate) occurs naturally (at non-toxic levels) in many food products, which humans may be exposed to on a daily basis without apparent harmful effects. As noted in Section VII, bisulfate/sulfate anions are readily water soluble and rapidly excreted without the formation of toxic metabolites.

As also noted previously in Section III, sodium bisulfate is already approved by EPA for residential non-food use as an antimicrobial active ingredient (toilet bowl sanitizer), which would not result in undue exposure and risks to infant and or adult populations. Additionally, in accordance with 40 CFR §180.920, sodium bisulfate is currently exempt from tolerance requirements when used as an acidifying/buffering agent in pesticide formulations applied to growing crops. There are no known issues with any possible residues and/or EPA mandated use restrictions.

2. Aggregate

EPA has not published a sodium bisulfate aggregate risk assessment.

3. Determination of Safety to U.S. Population

As previously noted, EPA has not reported toxicological endpoints of concern for the current non-food residential use and the use as an inert ingredient in pesticide formulations according to 40 CFR §180.920 applications. Based on this, EPA has determined that a quantitative risk assessment is not required for sodium bisulfate. A sodium bisulfate aggregate assessment has not been reported by EPA. As noted above, the anticipated food, drinking water and residential exposure should not be of concern since toxicological endpoints for risk assessment were not identified based on the available data reported in Sections III and VIII.

Moreover, it should not be anticipated that the use of sodium bisulfate in non-food residential pesticide formulations, as an inert ingredient in pesticide formulations according to 40 CFR §180.920 applications and the requested use as an inert ingredient in pesticide product formulations according to 40 CFR §180.9209(a) applications would result in special sensitivity of infants and children, as well as aggregate exposure. The inclusion of the uses supported by expanding the current 40 CFR §180.920 tolerance exemptions to include uses cited at 40 CFR §180.940(a) should not change this determination.

E. Cumulative Effects

Section 408(b)(2)(D)(9v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." Unlike pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not conducted a common mechanism of toxicity evaluation for sodium bisulfate.

JECFA (2010) confirms that bisulfate/sulfate anions do not constitute toxic metabolites. Thus, the Agency would assume that sodium bisulfate does not have a common mechanism of toxicity with other substances. As a result, any potential human health risks would be those that result only from the use of sodium bisulfate as a household use sanitizer for toilet bowls and as an inert ingredient in pesticide formulations applied to growing crops according to 40 CFR §180.920 applications.

SECTION IX. INTERNATIONAL TOLERANCES

There are currently no CODEX MRLs established for sodium bisulfate. JECFA has concluded that the ADI for sodium bisulfate should be "not assigned".

SECTION X. ENVIRONMENTAL RISK

The following is a summary of the environmental fate and risk information available for sodium bisulfate as reported by UNEP (2005):

> "In water sodium sulfate completely dissociates into sodium and sulfate ions. The ions cannot hydrolyse. In anaerobic environments sulfate is biologically reduced to (hydrogen) sulphide by sulfate reducing bacteria, or incorporated into living organisms as a source of sulphur, and thereby included in the sulphur cycle. Sodium sulfate is not reactive in aqueous solution at room temperature. Sodium sulfate will completely dissolve, ionise and distribute across the entire planetary "aquasphere". Some sulfates may eventually be deposited, the majority of sulfates participate in the sulphur cycle in which natural and industrial sodium sulfate are not distinguishable. The BCF of sodium sulfate is very low and therefore significant bioconcentration is not expected. Sodium and sulfate ions are essential to all living organisms and their intracellular and extracellular concentrations are actively regulated. However, some plants (e.g. corn and *Kochia Scoparia*), are capable of accumulating sulfate to concentrations that are potentially toxic to ruminants. Algae were shown to be the most sensitive to sodium sulfate with an EC_{50} 120h = 1,900 mg/l. For invertebrates, *(Daphnia magna),* the EC_{50} 48h = 4,580 mg/l and fish appeared to be the least sensitive with a LC_{50} 96h = 7,960 mg/l for *Pimephales promelas*. Activated sludge showed a very low sensitivity to sodium sulfate. There was no effect up to 8 g/l. Sodium sulfate is not very toxic to terrestrial plants. *Picea banksiana* was the most sensitive species, an effect was seen at 1.4 g/l. Sediment dwelling organisms were not very sensitive either, with an LC_{50} 96h = 660 mg/l for *Trycorythus sp*. Overall, it can be concluded that sodium sulfate has no acute adverse effect on aquatic and sediment dwelling organisms. Toxicity to terrestrial plants is also low."

Ecological Structure Activity Relationships (ECOSAR) modeling (Appendix XI) was conducted to confirm and provide supplemental data for potential toxicity to aquatic organisms (fish and invertebrates) and plants (algae). ECOSAR is a highly conservative model that is based on Structure to Activity (SAR) analyses of molecular fragments. Overall, the conservative ECOSAR modeling results indicate a low potential for toxicity to aquatic organisms. Additionally, the proposed indoor inert ingredient use will not result in any additional environmental exposure, especially in consideration of the current EPA approved 40 CFR §180.920 uses.

SECTION XI. PROPOSED EXEMPTION FROM TOLERANCE

The petitioner, Ecolab, Inc., proposes to amend 40 CFR §180.940(a) to establish an exemption from the requirement of a tolerance for residues of the inert ingredient sodium bisulfate when

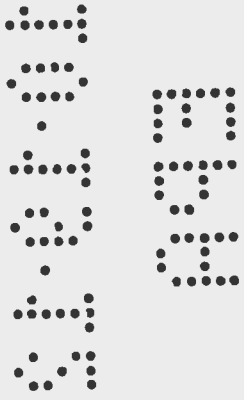
used as an inert ingredient in an antimicrobial pesticide formulation applied to food contact surfaces in public eating places, dairy-processing equipment, and food-processing equipment and utensils.

Inert Ingredient	CAS Reg. No.	Limits
Sodium Bisulfate	7681-38-1	None

SECTION XII. REGULATORY CONCLUSIONS AND REASONABLE GROUNDS

The data provided herein support that sodium bisulfate as an inert ingredient in 40 CFR §180.940(a) applications can be used safely in accordance with the required FQPA standard of "reasonable certainty of no harm."

Sodium bisulfate is ubiquitous in nature and occurs naturally in many food products. Ecolab emphasizes that the current sodium bisulfate 40 CFR §180.920 pesticide inert, EPA approved pesticide active ingredient registrations and FDA food additive uses have not represented undue risk to sensitive and adult US populations. The expansion of the 40 CFR §180.920 tolerance exemption should not change EPA's conclusion that sodium bisulfate can be used safely in accordance with the 40 CFR §180.840(a) applications.



SECTION XIII. REFERENCES

California Environmental Protection Agency Department of Pesticide Regulation Medical Toxicology Branch Summary of Toxicology Data Sodium Bisulfate, 2002. Chemical Code # 905, Tolerance # 50263

Fan X, Sokorai KJ, Liao CH, Cooke P, Zhang HQ., 2009. Antibrowning and antimicrobial properties of sodium acid sulfate in apple slices. J Food Sci.;74: 485-92.

Stephen Mixon, Director of Operations, Advanced Food Technologies, LLC., Letter to Antonia Mattia Office of Food Additive Safety, FDA dated October 12, 2011, "GRAS Notification for sulfuric acid and sodium sulfate blend used as an antimicrobial in meat and poultry processing."

Alan M. Rulis, FDA Director Office of Premarket Approval, Letter to Ms. Betty J. Pendleton Jones-Hamilton Co., dated June 5, 1998, GRAS Notice No. GRN 000003, Docket No. 98S-0104

UNEP 1995 SIDS Sodium Sulfate

US EPA Registration Eligibility Document, 1993. Mineral Acids Case 4064.

World Health Organization (WHO) Food Additives Series: 44 Safety Evaluation Of Certain Food Additives And Contaminants, 2000.

World Health Organization (WHO) Food Additives Series: 62 Safety Evaluation Of Certain Food Additives And Contaminants, 2010a. Pages 237-247

WHO Technical Report Series 956 71st Report of the Joint FAO/WHO Expert Committee on Food Additives, 2010b Page 43-46.

APPENDICES

Appendix I. EPA RED Mineral Acids, 1993

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onmental Protection
Agency

Prevention, Pesticides
And Toxic Substances
(7508W)

EPA-738-F-93-025
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EPA R.E.D. FACTS

Mineral Acids

Pesticide Reregistration

All pesticides sold or distributed in the United States must be registered by EPA, based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides which were first registered years ago be reregistered to ensure that they meet today's more stringent standards.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. The Agency imposes any regulatory controls that are needed to effectively manage each pesticide's risks. EPA then reregisters pesticides that can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA announces this and explains why in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED for the case mineral acids, which contains the active ingredients hydrogen chloride, phosphoric acid, sodium bisulfate, and sulfuric acid.

Use Profile

The four pesticide active ingredients that comprise the mineral acids reregistration case are used as tuberculocides, disinfectants, sanitizers, virucides, fungicides, desiccants and antimicrobials. **Hydrogen chloride** is used as a disinfectant for bathroom, commercial, industrial, institutional, hospital, laboratory, morgue, refuse, cafeteria and veterinary premises, on surgical instruments, animal cages, swimming pool tile and drinking fountains, and for dishes, glassware and utensils. **Phosphoric acid** is used as an antimicrobial in industrial processing water, empty mushroom houses, food and dairy premises and processing plant equipment, animal kennels, hospitals and morgues, and bathroom premises. **Sodium bisulfate** is used as a disinfectant for toilet bowls. **Sulfuric acid** is used as a desiccant on potato crops, and as a sanitizer for food processing and dairy facilities, equipment and utensils. Sulfuric acid is the largest volume chemical produced in the United States, and is used primarily for non-pesticidal purposes.

These active ingredients are formulated as emulsifiable, soluble and solid concentrates, ready-to-use liquids, pellets/tablets, solids and impregnated material.

Regulatory History

The mineral acids were first registered as pesticides in the United States during the 1950s. Currently, 212 products are registered which contain the mineral acids as active ingredients.

Human Health Assessment

Toxicity

All four of the mineral acids are corrosive to the eyes and all except sodium bisulfate are corrosive to the skin; they have been placed in Toxicity Category I indicating the greatest degree of acute toxicity for eye and dermal irritation effects. Sulfuric acid also is extremely acutely toxic by the inhalation route, and has been placed in Toxicity Category I for inhalation effects. The mineral acids otherwise are moderately acutely toxic, and are placed in Toxicity Category III (on a scale of I to IV) for acute oral and dermal effects. (Sulfuric acid, however, is placed in Toxicity Category II for acute oral toxicity.)

Dietary Exposure

Sulfuric acid is the only mineral acid that has a registered food use, that is, application to potato vines five or more days prior to harvest to desiccate the vines and make harvesting less difficult. Sulfuric acid is exempt from the requirement of a tolerance for this use. Sulfuric acid was granted an exemption from tolerance requirements because it is rapidly degraded in the environment to sulfate salts, which are of no toxicological concern and are Generally Recognized as Safe (GRAS) by the Food and Drug Administration. There are no human dietary concerns associated with the potato vine use of sulfuric acid.

Occupational and Residential Exposure

Hydrogen chloride and phosphoric acid, which are used mainly as antimicrobials to sanitize food and dairy processing plants, are applied as wipe-on surface treatments, sprays, and circulate in place (CIP) treatments. Sodium bisulfate, used as a disinfectant, is a solid soluble concentrate which is brushed/swabbed onto the interior surfaces of toilet bowls. Sulfuric acid, like the first two chemicals, is used to sanitize milk lines and food processing surfaces by wipe-on and CIP treatments. In addition, concentrated sulfuric acid (93%) is used to desiccate potato vines prior to harvest. A Restricted Use Pesticide, it is applied by certified applicators using special ground boom type equipment.

When the four mineral acids are used as antimicrobials, only dilute solutions are applied to surfaces. Because the chemicals are applied at low concentrations, mixer/loader/applicator exposure both during and post-application is likely to be negligible.

The use of concentrated sulfuric acid as a potato vine desiccant may result in dermal and inhalation exposure of workers, during and after treatment, potentially causing severe irritation to mucous membranes and

skin. To avoid these effects, product labels must be updated to require adequate personal protective equipment. In addition, the registrant must explain the basis for the existing 5-day reentry interval, and demonstrate that it is sufficiently protective to post-application workers.

Human Risk Assessment

The four mineral acids pose no human dietary risks. People may be exposed to these chemicals when they are used as antimicrobials, however this exposure involves such dilute solutions that it is believed to be inconsequential. The use of concentrated sulfuric acid as a potato desiccant results in high potential for worker exposure and risk. EPA is maintaining the existing 5-day reentry interval into treated potato fields, and is requesting a rationale for this interval. In addition, labels must be updated to require use of adequate personal protective equipment and clothing, as specified in the Worker Protection Standard.

Environmental Assessment

EPA has predicted the environmental fate of the mineral acids in the environment using commonly available sources of information, as well as basic chemistry. The Agency is not able to determine, at this time, if the use of sulfuric acid as a desiccant on potato vines is eligible for reregistration. The Agency is concerned about the risk to terrestrial wildlife, and is not aware of any acceptable methods to mitigate the risk. In order to determine its eligibility, the Agency will be assessing the benefits of sulfuric acid for this use. Once this is done, the Agency will make a finding of whether this use is eligible for reregistration and whether any further regulatory action is required.

Environmental Fate

The mineral acids generally dissociate and release hydrogen ions in the environment, thus increasing the pH of soil or water.

Ecological Effects

For all mineral acids and uses except the use of sulfuric acid as a potato vine desiccant, adequate information is available to predict the effects on living organisms, so all normally required avian and aquatic studies were waived. If the mineral acids, diluted or undiluted, came into contact with birds, they would cause severe dermal toxicity to areas not covered by feathers. All of the mineral acids pose a potential hazard to the aquatic environment, due to their ability to change the pH of receiving waters. Such changes in pH can have serious adverse effects on fish.

Ecological Effects Risk Assessment

Avian species are at risk from direct exposure to mineral acids, and such exposure must be avoided. Mineral acids also can cause significant changes in pH, which are harmful to aquatic species and also must be avoided. These exposures also may be harmful to endangered species.

The risks posed by the mineral acids will be mitigated by product labeling, as specified in the RED document.

The use of sulfuric acid as a desiccant on potato vines, however, poses significant hazard to birds and other terrestrial wildlife. Since there are no known practical mitigation measures, this use is not eligible for reregistration, at this time.

Additional Data Required

EPA is requiring product-specific data, including product chemistry and acute toxicity studies, as well as revised Confidential Statements of Formula (CSF) and revised labeling, for reregistration of products containing the mineral acids.

Product Labeling Changes Required

All end-use mineral acid products must comply with EPA's current pesticide labeling requirements. In addition:

- **Compliance with Worker Protection Standard (WPS)** - Products used in the production of an agricultural plant or on any agricultural establishment (farm, forest, nursery or greenhouse) must comply with the labeling requirements of:
  - PR Notice 93-7, "Labeling Revisions Required by the Worker Protection Standard (WPS)," and
  - PR Notice 93-11, "Supplemental Guidance for PR Notice 93-7."

Unless specifically directed in the RED, all statements required by these two PR Notices must appear on product labeling exactly as instructed in the Notices. Labels must be revised by April 21, 1994, for products distributed or sold by the primary registrant or supplementally registered distributors, and by October 23, 1995, for products distributed or sold by anyone.

- **Personal Protective Equipment and Reentry Requirements** - Sulfuric acid, when used as a potato vine desiccant, has a potential for dermal and inhalation exposure to mixer/loader/applicators both during and after application. The current label allows for post-application reentry of workers when wearing appropriate personal protective clothing and equipment. Otherwise post-application reentry is not permitted for 5 days. The posting of notices when fields are treated is required.

- **Effluent Discharge Statement** - All end-use and manufacturing use products that may be contained in an effluent discharged to the waters of the United States must bear the following statement:

> "Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying

the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."

- **Wildlife Protection Statement** - Products containing hydrogen chloride or phosphoric acid and used in swimming pools must bear the following statement:

"This pesticide is toxic to wildlife. Do not contaminate water when disposing of equipment wash water or rinsate."

Regulatory Conclusion

The use of currently registered pesticide products containing mineral acids, except use of sulfuric acid as a desiccant on potato vines, in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products are eligible for reregistration.

These products will be reregistered once the required product specific data, revised Confidential Statements of Formula and revised labeling are received and accepted by EPA. Products which also contain other active ingredients will be reregistered after the other active ingredients also are determined to be eligible for reregistration.

The use of sulfuric acid on potato vines will be subject to further assessment of its benefits for this use. Once this is done, the Agency will make a finding of whether this use is eligible and whether any further regulatory action is required.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for Mineral Acids during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED or to submit written comments, please contact the Pesticide Docket, Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Following the comment period, the Mineral Acids RED will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-487-4650.

For more information about EPA's pesticide reregistration program, the Mineral Acids RED, or reregistration of individual products containing mineral acids, please contact the Special Review and Reregistration Division (7508W), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000.

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticides Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, between 8:00 am and 6:00 pm, Central Time, Monday through Friday.

REREGISTRATION ELIGIBILITY DECISION

MINERAL ACIDS

LIST D

CASE 4064

ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS
SPECIAL REVIEW AND REREGISTRATION DIVISION

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GLOSSARY OF TERMS AND ABBREVIATIONS

a.i.	Active Ingredient
CAS	Chemical Abstracts Service
CSF	Confidential Statement of Formula
EEC	Estimated Environmental Concentration. The estimated pesticide concentration in an environment, such as a terrestrial ecosystem.
EP	End-Use Product
EPA	U.S. Environmental Protection Agency
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
GRAS	Generally Recognized As Safe as designated by FDA
HDT	Highest Dose Tested
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LD_{lo}	Lethal Dose-low. Lowest Dose at which lethality occurs
LEL	Lowest Effect Level
LOEL	Lowest Observed Effect Level
MP	Manufacturing-Use Product
MPI	Maximum Permissible Intake

GLOSSARY OF TERMS AND ABBREVIATIONS

MOE	Margin Of Exposure (PAD)
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.
N/A	Not Applicable
NPDES	National Pollutant Discharge Elimination System
NOEL	No Observed Effect Level
OPP	Office of Pesticide Programs
PADI	Provisional Acceptable Daily Intake
ppm	Parts Per Million
Q^*_1	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RED	Reregistration Eligibility Decision
RfD	Reference Dose
RS	Registration Standard
TD	Toxic Dose. The dose at which a substance produces a toxic effect.
TC	Toxic Concentration. The dose at which a substance produces a toxic effect.
TMRC	Theoretical Maximum Residue Contribution.

EXECUTIVE SUMMARY

This Reregistration Eligibility Decision (RED) addresses pesticide uses of hydrogen chloride, phosphoric acid, sodium bisulfate, and sulfuric acid in the chemical case mineral acids. Products containing these active ingredients are used as tuberculocides, disinfectants, sanitizers, virucides, fungicides, desiccants, and antimicrobials. Registered use sites include commercial and industrial water cooling tower systems, swimming pool water systems, eating establishments, eating establishment equipment/utensils, food processing plant equipment, animals (laboratory/research/commercial/institutional) premise treatment, bathroom premises/hard surfaces, refuse/solid waste sites, toilet bowls, urinals, a variety of disinfectant and cleaning uses (hospital, agricultural, dairy), and mushroom houses. The mineral acid active ingredients are formulated as emulsifiable concentrates, soluble concentrates/liquids, and liquid-ready to use products.

The U.S. Environmental Protection Agency has determined that, except for the sulfuric acid potato vine desiccant use, the uses of these four active ingredients as currently registered will not cause unreasonable risk to humans or the environment and these uses are eligible for reregistration. The Agency is not able to determine, at this time, if the use of sulfuric acid as applied to potato vines is eligible for reregistration. The Agency is concerned about the risk to terrestrial wildlife and is not aware of any acceptable methods to mitigate the risk. In order to determine its eligibility, the Agency will be assessing the benefits of sulfuric acid for this use. Once this is done, the Agency will make a finding of whether this use is eligible for reregistration and whether any further regulatory action is required.

Before reregistering the products containing these mineral acids, the Agency is requiring that product specific data, revised Confidential Statements of Formula (CSF) and revised labeling be submitted within eight months of the issuance of this document. These data include product chemistry for each registration and acute toxicity testing. After reviewing these data and any revised labels and finding them acceptable in accordance with Section 3(c)(5) of FIFRA, the Agency will reregister a product. Those products which contain other active ingredients will be eligible for reregistration only when the other active ingredients are determined to be eligible for reregistration.

I. INTRODUCTION

In 1988, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act provides a schedule for the reregistration process to be completed in nine years. There are five phases to the reregistration process. The first four phases of the process focus on identification of data requirements to support the reregistration of an active ingredient and the generation and submission of data to fulfill the requirements. The fifth phase is a review by the U.S. Environmental Protection Agency (referred to as "the Agency") of all data submitted to support reregistration.

FIFRA Section 4(g)(2)(A) states that in Phase 5 "the Administrator shall determine whether pesticides containing such active ingredient are eligible for registration" before calling in data on products and either reregistering products or taking "other appropriate regulatory action." Thus, reregistration involves a thorough review of the scientific data base underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential hazards arising from the currently registered uses of the pesticide; to determine the need for additional data on health and environmental effects; and to determine whether the pesticide meets the "no unreasonable adverse effects" criterion of FIFRA.

This document presents the Agency's decision regarding the reregistration eligibility of the registered uses of hydrogen chloride, phosphoric acid, sodium bisulfate, and sulfuric acid in the chemical case mineral acids. The document consists of six sections. Section I is the introduction. Section II describes these mineral acids, their uses, data requirements and regulatory history. Section III discusses the human health and environmental assessment based on the data available to the Agency. Section IV presents the reregistration decision for mineral acids. Section V discusses the reregistration requirements for mineral acids. Finally, Section VI is the Appendices which support this Reregistration Eligibility Decision. Additional details concerning the Agency's review of applicable data are available on request.

II. CASE OVERVIEW

A. Chemical Overview

The following active ingredients are covered by this Reregistration Eligibility Document:

1. **Chemical Name:** Hydrogen chloride

   - **Chemical Family:** Inorganic acid
   - **CAS Registry Number:** 7647-01-0
   - **OPP Chemical Code:** 045901
   - **Empirical Formula:** HCl
   - **Trade and Other Names:** Hydrochloric acid

2. **Chemical Name:** Phosphoric acid

   - **Chemical Family:** Inorganic acid
   - **CAS Registry Number:** 7664-38-2
   - **OPP Chemical Code:** 076001
   - **Empirical Formula:** H_3PO_4
   - **Trade and Other Names:** Orthophosphoric acid
     Phosphorous oxide

3. **Chemical Name:** Sodium bisulfate

   - **Chemical Family:** Inorganic acid
   - **CAS Registry Number:** 7681-38-1
   - **OPP Chemical Code:** 073201
   - **Empirical Formula:** $HNaO_4S$
   - **Trade and Other Names:** Sodium acid sulfate, Sodium hydrogen sulfate, and Sodium pyrosulfate

4. **Chemical Name:** Sulfuric acid

- **Chemical Family:** Inorganic acid
- **CAS Registry Number:** 7664-93-9
- **OPP Chemical Code:** 078001
- **Empirical Formula:** H_2SO_4
- **Trade and Other Names:** Oil of vitriol

B. Use Profile

The following is information on the current registered uses with an overview of use sites and application methods. A detailed table of these uses of hydrogen chloride, phosphoric acid, sodium bisulfate, and sulfuric acid is in Appendix A.

1. For Hydrogen chloride:

Type of Pesticide:

Tuberculocide, disinfectant (bactericide/germicide/purifier, limited, general or broad-spectrum, hospital or medical), sanitizer, virucide, fungicide/fungistat, and microbicide/microbiostat (slime-forming bacteria)

Use Sites:

Indoor non-food - Animals (Laboratory/Research)*, animal kennels/sleeping quarters (commercial), commercial/institutional/industrial premises/equipment (indoor), commercial storage/warehouse premises indoor), commercial transportation facilities-nonfeed/nonfood, donkeys*, eating establishments food handling areas (non-food contact), eating establishments food serving areas (non-food contact), eating establishments non-food areas (non-food contact), fox*, goats (wool/angora animal)*, horses (show/race/special/ponies)*, laundry equipment, mink*, mules (work)*, nutria*, rabbits*, sheep*, specialized animals*, tobacco processing plant premises/equipment

*Animal equipment and premise treatment.

Aquatic non-food residential - Swimming pool water systems [water-related surface treatment]

Indoor food - Dairies/cheese processing plant premises (non-food contact), eating establishments, eating establishment equipment/utensils (food contact), feed mills/feed processing plants**, fish/seafood processing plant premises (non-food contact), food catering facilities premises, food dispensing equipment/vending machines**, food/grocery/marketing/storage/distribution facility premises, food marketing/storage/distribution equipment/utensils (food contact)**, food processing plant equipment (food contact), food processing plant premises (non-food contact), meat/fish market premises, meat processing plant premises (non-food contact), poultry processing plant premises (non-food contact)

**For use on non-food contact surfaces only.

Indoor medical - Barber/beauty shop equipment (barber chairs/cabinets), barber/beauty shop instruments (shavers/scissors), cuspidors/spittoons, hospital/medical institution premises (human/veterinary), hospital conductive floors, hospital/medical institution critical premises (burn wards), hospital/medical institution noncritical premises, hospital/medical institution patient premises, hospital critical items (surgical instruments/pacemakers), hospital janitorial equipment, hospital semicritical items (catheters/inhalation equipment), hospital noncritical items (bedpans/furniture), morgues/mortuaries/autopsy/embalming room premises, morgues/mortuaries/autopsy/embalming equipment, morgues/mortuaries/autopsy/embalming instruments

Indoor residential - bathroom premises/hard surfaces, household trash compactor/food disposals, incinerators, portable/chemical toilets/latrine buckets, refuse/solid waste containers (garbage cans), refuse/solid waste sites (indoor), refuse/solid waste transportation facilities/handling equipment, toilet bowls (interior surfaces), toilet tanks/water closets water, urinals (interior surfaces), vehicular holding tanks

Target Pests:

Mycobacterium tuberculosis, Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli, Streptococcus faecalis, Shigella dysenteriae, Shigella flexneri, Shigella sonnei, Salmonella typhi, Salmonella cholerasuis, Salmonella typhimurium, Proteus vulgaris, Enterobacter aerogenes, Enterobacter faecalis, Serratia marcescens, Trichophyton interdigitale, HIV-1 (AIDS virus), Influenza A2 virus, *Herpes simplex*, Type 1 polio virus, Canine parainfluenza virus, and Canine reovirus.

Formulation Types Registered:

Type: End use

Form: Emulsifiable concentrate, soluble concentrate/liquid, liquid - ready to use

Method and Rates of Application:

Types of Treatment

Indoor non-food - Disinfectant for laboratory animal, donkey, fox, goat, horse, mink, mules, nutria, rabbit, sheep, and zoo animal premises - animal equipment treatment, premise treatment, surface treatment - 90,000 to 237,000 ppm a.i. by weight; 10 ppm a.i. by volume (for laboratory animal premises only).
Disinfectant for animal kennels, warehouses, vehicles, commercial and industrial premises and equipment, laundry equipment, and eating establishment non-food areas - mop, scrub, sponge-on, surface treatment, swab, transportation vehicle treatment, brush-on, wipe-on - 90,000 to 237,000 ppm a.i. by weight; 30,000 ppm a.i. by volume.

Aquatic non-food residential - Disinfectant for swimming pool tile - water-related surface treatment - 47,500 ppm a.i. by weight.

Indoor food - Disinfectant for eating establishment premises and equipment/ utensils, food processing plant equipment - premise treatment, immersion, mop, spray - 5 to 86 ppm a.i. by volume.
Disinfectant for non-food contact areas of meat and fish markets, food processing plants, dairy processing plants, feed mills, meat processing plants, poultry processing plants, seafood processing plants, catering facilities, food dispensing equipment and vending machines, and food marketing, storage, and distribution equipment -brush-on, mop, scrub, sponge-on, surface treatment, swab, wipe-on -90,000 to 237,000 ppm a.i. by weight; 30,000 ppm a.i. by volume.

Indoor medical - Disinfectant for barber and beauty shop equipment and instruments, cuspidors and spittoons, hospital janitorial equipment, hospital noncritical items, hospital critical and noncritical premises, hospital patient premises, embalming equipment and instruments, and morgues - mop, scrub, sponge-on, surface treatment, swab, wipe-on, immersion - 90,000 to 237,000 ppm a.i. by weight; 5 to 10 ppm a.i. by volume.
Disinfectant for hospital conductive floors - premise treatment - 5 ppm a.i. by volume.

Disinfectant for hospital critical items - immersion - 30 ppm a.i. by volume.
Disinfectant for hospital semicritical items - not on label - 5 ppm a.i. by volume.

Indoor residential - Disinfectant for trash compactors, food disposals, incinerators, portable toilets, garbage cans, refuse transportation and handling equipment, and vehicular holding tanks - mop, scrub, sponge-on, swab, wipe-on, surface treatment - 90,000 to 237,000 ppm a.i. by weight.
Disinfectant for bathroom surfaces - brush-on, mop, not on label, pour-on, premise treatment, scrub, sponge-on, surface treatment, swab, wipe-on - 85000 to 237000 ppm a.i. by weight; 5 to 30000 ppm a.i. by volume.
Porous surfaces - 6000 ppm a.i. by volume.
Disinfectant for toilets and urinals - brush-on, flush treatment, mop, not on label, pour-on, sponge-on, surface treatment, swab, scrub - 47100 to 260000 ppm a.i. by weight; 117 to 24687 ppm a.i. by volume.
Disinfectant for toilet tanks - surface treatment - 90,000 ppm a.i. by weight.

Equipment - Brush, mop, tank, sprayer, sponge, swab, cloth, package applicator, bowl mop, not on label.

Method and Rate - See Types of Treatment.

Timing - Not specified.

Use Practice Limitations:

Some solutions have a rich amber color and as long as the color remains, germicidal action is assured. Once the color has disappeared, the solution should be made fresh. Do not use on marble or resilient tile floors, enamel surfaces, or chrome or nickel-plated plumbing fixtures. Do not use with bleach.

2. For Phosphoric acid

Type of Pesticide: Antimicrobial

Mechanism of Action: Acidifies, thus preventing or delaying growth of target organisms

Use Sites:

Aquatic nonfood industrial - Industrial processing water

Greenhouse food crop - Mushroom houses-empty premises/equipment

Indoor food - Agricultural/farm premises, dairies/cheese processing plant equipment, dairy farm milk handling facilities/equipment, dairy farm milking equipment, eating establishments premises/equipment/ utensils, egg handling equipment and washing treatments, food dispensing equipment, food marketing/storage/distribution equipment/utensils, food processing plant equipment/premises, human drinking water systems, livestock, meat processing plant equipment/premises, poultry, poultry drinking water, poultry processing plant equipment/premises

Indoor nonfood - Agricultural/farm equipment, animal kennel/sleeping quarters, commercial/institutional/industrial premises/equipment, eating establishment and food serving areas, egg plants/hatcheries, mushroom houses-empty premises/equipment

Indoor medical - Hospital critical/semicritical/noncritical items/floors, hospitals critical/noncritical/patient premises, hospitals/medical institutions premises, morgues/mortuaries equipment/premises

Indoor residential - Bathroom premises, pet living/sleeping quarters, refuse/solid waste containers, toilet bowls/urinals

Target Pests:

Staphylococcus aureus, Escherichia coli, Mycobacterium tuberculosis, Streptococcus pyogenes, Streptococcus faecalis, Streptococcus salivarius, Corynebacterium diptheriae, Salmonella choleraesuis, Salmonella paratyphi, Salmonella schottmuelleri, Neisseria elongata, Acinetobacter calcoaceticus, Shigella dysenteriae, Enterobacter aerogenes, Proteus vulgaris, Proteus mirabilis, Pseudomonas aeruginosa, Pseudomonas cepacia, Klebsiella pneumoniae, Serratia marcescens, Staphylococcus aureus (penicillin resistant), *Bacillus subtilis* spores, *Clostridium tetani* spores, *Clostridium sporogenes* spores, *Herpes simplex*, Influenza A_2 (Asian), *Candida albicans, Trichophyton mentagrophytes, Aspergillus niger, Salmonella typhosa* (ATCC 6539), *Escherichia coli,* (ATCC 11229), *Listeria monocytogenes* (ATCC No. 15313), *Staphylococcus aureus,* (ATCC 6538), *Herpes simplex* type 1, Influenza A2, influenza A2/Hong Kong, Newcastle disease, vaccinia, adenovirus types 2 and 3, Human Immunodeficiency virus type I (AIDS virus), odor causing bacteria, mildew and pathogenic fungi (*Trichophyton mentagrophytes,*

Trichophyton interdigitale, athlete's foot fungi), mold; bacteria and algae, slime-forming bacteria and fungi, foulbrood disease, *Mycobacterium* spp., polioviruses, lipophilic viruses.

Formulation Types Registered:

Single Active Ingredient Products
Pelleted/tableted--0.13%
Soluble concentrate/liquid--15 to 75.5%
Liquid ready to use--25%

Multiple Active Ingredient (a.i.) Products
Impregnated material--2% + 1 other a.i.
Solid concentrate/liquid--0.632 to 57% + 1 to 4 other a.i.
Liquid ready to use--0.85 to 45% + 1 other a.i.
Solid concentrate/solid--29.3% + 1 other a.i.

Methods and Rates of Application:

Aquatic nonfood industrial - Industrial processing water 35-250 ppm a.i. by vol

Greenhouse food crop -Mushroom houses-empty premises/equipment 150 ppm a.i. by vol

Indoor food - Agricultural/farm premises: 625 ppm a.i. by vol; dairies/cheese processing plant equipment: 146 ppm a.i. by weight, 106 - 3000 ppm a.i. by vol; dairies/cheese processing plant premises: 148 - 619 ppm a.i. by vol; dairy farm milk handling facilities/equipment: 94 - 4688 ppm a.i. by vol; dairy farm milking equipment: 47 - 4688 ppm a.i. by vol, eating establishments premises/equipment/utensils: 73 - 146 ppm a.i. by weight, 106 - 3516 ppm a.i. by vol; egg handling equipment: 148 ppm a.i. by vol; egg washing treatments: 293 ppm a.i. by vol; food dispensing equipment: 732 - 3516 ppm a.i. by vol; food marketing/storage/distribution equipment/utensils: 625 ppm a.i. by vol; food processing plant equipment: 146 ppm a.i. by weight, 25 - 3516 ppm a.i. by vol; food processing plant premises: 625 - 750 ppm a.i. by vol; human drinking water systems (specific site is drinking fountains): 66,666 ppm a.i. by vol, human drinking water systems - water softener salt: 202,561 ppm a.i. by vol, water softener resin beds: 1300 ppm by weight; livestock (housing and equipment): 638 ppm a.i. by vol; meat processing plant equipment: 125 - 2637 ppm a.i. by vol; meat processing plant premises: 527 - 625 ppm a.i. by vol; poultry (housing and equipment): 625 - 638 ppm a.i by vol; poultry drinking water: 125 ppm a.i by vol; poultry processing plant equipment: 125 - 2637 ppm a.i. by vol; poultry

processing plant premises: 527 - 625 ppm a.i. by vol.

Indoor nonfood - Agricultural/farm equipment: 625 - 3750 ppm a.i. by vol; animal kennel/sleeping quarters: 527 ppm a.i. by vol; commercial/institutional/industrial premises/equipment: 305 - 1500 ppm a.i. by vol; eating establishment and food serving areas: 146 ppm a.i. by weight; egg handling equipment: 527 ppm a.i. by vol; egg plants/hatcheries/brooder rooms/shoe baths: 527 - 3750 ppm a.i. by vol; mushroom houses-empty premises/equipment: 449 ppm a.i. by vol.

Indoor medical - Hospital conductive floors: 625 - 738 ppm a.i. by vol; hospital critical items: 309 - 879 ppm a.i. by vol, 85,000 ppm a.i. by weight; hospital semicritical items: 703 - 2125 ppm a.i. by vol, 85,000 ppm a.i. by weight; hospital noncritical items: hospital non-conductive floors: 250 - 1328 ppm a.i. by vol; hospitals critical premises: 335 - 1328 ppm a.i. by vol; hospital noncritical premises: 879 - 1500 ppm a.i. by vol; hospital patient premises: 638 - 1500 ppm a.i. by vol; hospitals/medical institutions premises: 305 - 1500 ppm a.i. by vol, 120,000 ppm a.i. by weight; morgues/mortuaries equipment/premises: 750 - 1328 ppm a.i. by vol.

Indoor residential - Bathroom premises: 531 - 82000 ppm a.i. by vol, 32000 - 146200 ppm a.i. by weight; pet living/sleeping quarters: 305 ppm a.i. by vol; refuse/solid waste containers: 750 ppm a.i. by vol; toilet bowls: 1403 - 20833 ppm a.i. by vol, 21000 - 450000 ppm a.i. by weight; urinals: 664 - 18750 ppm a.i. by vol, 21000 - 450000 ppm a.i. by weight

Use Practice Limitations: None

3. For Sodium bisulfate

Type of Pesticide: Disinfectant

Use Sites: Indoor residential - Interior surfaces of toilet bowls

Target Pests: Household and Odor-causing bacteria, *Staphylococcus spp.*

Formulation Types Registered:

Type: End use

Form: Solid soluble concentrate

Method and Rates of Application:

Types of treatment: Sprinkle

Equipment: Brush, Swab

Timing: As needed

Rate of application: From 30400 up to 49248 ppm a.i. by weight

Use Practices Limitations: None

4. For Sulfuric acid

Type of Pesticide: Sanitizer, desiccant

Mechanism of Action: Acidifies

Use Sites:

Terrestrial food + feed crop - White potato

Indoor food - Dairy/cheese processing plant equipment, dairy farm milking equipment and milk handling facilities/equipment, eating establishments equipment/utensils, food marketing/storage/distribution equipment/utensils, food processing plant equipment

Target Pests: Animal pathogenic bacteria (sanitizer use)

Formulation Types Registered:

Single Active Ingredient Products
Liquid ready to use--93% (desiccant use)

Multiple Active Ingredient (a.i.) Products
Soluble concentrate/liquid--9.5% + 4 other a.i. (sanitizer use)

Methods and Rates of Application:

Liquid ready to use - At preharvest of potatoes, apply desiccation treatment at 285 to 391 lbs a.i./acre.

Soluble concentrate/liquid - Circulate-in-place or equipment treatment at 1 fl oz product/6 gal water for a minimum contact time of 2 min.

Use **Practices Limitations:** Do not apply within 5 days of harvest of potatoes.

C. Regulatory History

Phosphoric acid and hydrogen chloride were registered in the United States as sanitizers and disinfectants as early as 1958. There are currently 91 phosphoric acid products and 62 hydrogen chloride products registered for use in or on agricultural premises, food establishments, commercial/institutional/residential locations, and hospital/medical institutions on a variety of hard surfaces such as urinals/toilets, mushroom houses, dairy equipment, food processing equipment, etc. in indoor and outdoor applications.

Sodium bisulfate was registered in the U.S. as a sanitizer and disinfectant in 1968. There are currently 12 products registered in the U.S. All of these products are registered for use as toilet bowl cleaners/sanitizers.

Sulfuric acid was registered as a desiccant/herbicide in the U.S. as early as 1971. Sulfuric acid was exempted from a residue tolerance requirement for this use (40 CFR § 180.1019). A food processing sanitizer emulsion product utilizing sulfuric acid in combination with other acids was registered in 1992. (FFDCA, § 178.1010 (b)(c), amended 1992.) There are currently six products registered for agricultural uses (desiccant/herbicide), and one product (in combination with other active ingredients) registered as a sanitizer.

Historically, certain phosphoric acid products and certain other liquid chemical germicides have been regulated both as pesticides under the FIFRA and as devices under the FFDCA. In an effort to resolve the confusion and burden of dual regulation, a Memorandum of Understanding (MOU) was signed on June 4, 1993 between EPA and the Food and Drug Administration (FDA). The objectives of the MOU are to (1) stimulate both Agencies to undertake rulemaking to permanently vest exclusive jurisdiction for certain categories of chemical germicides in each Agency and (2) serve as interim guidance designed to minimize duplicative regulatory requirements between the two Agencies until the rulemaking is complete.

The MOU separates the liquid chemical germicides into the following two categories based on their use patterns and efficacy claims: (1) sterilants and (2) general purpose disinfectants. Sterilants, under this agreement, refer to those chemical germicides used to reprocess reusable critical and semicritical devices as defined by the Centers for Disease Control (CDC). Critical devices are devices that are introduced directly into the human body, either into or in contact with the bloodstream or normally sterile areas of the body. Semicritical devices are those which contact intact mucous

membranes but which do not ordinarily penetrate the blood barrier or otherwise enter normally sterile areas of the body. General disinfectants are defined as all remaining types of public health liquid chemical germicides bearing non-sterilant claims for use on non-critical surfaces.

The MOU outlines the future separate regulation of liquid chemical germicides as either pesticides under FIFRA or devices under FFDCA by granting each Agency primary jurisdiction over one of the two categories. All products which bear sterilant label claims and can be used on critical or semicritical surfaces will be regulated by FDA as devices. In addition, many sterilant products have claims which correspond to a high level disinfectant use pattern. These claims will also be regulated by FDA for the sterilant products. EPA will regulate the general purpose disinfectants.

Because the MOU does not change the statutory authority granted under FIFRA and FFDCA, both Agencies will continue to have jurisdiction over all liquid chemical germicides and will continue registration and premarket approval until rulemaking has been completed. However, the MOU reduces the regulatory burden by stating that the required data to support efficacy claims and product performance need only be submitted and reviewed by the Agency with primary jurisdiction as defined above. In the case of the phosphoric acid products, EPA has primary jurisdiction and the conditions of reregistration must be fulfilled and required data submitted as presented in Appendices F and G.

A copy of the signed EPA/FDA MOU is attached as Appendix H.

III. SCIENCE ASSESSMENT

A. Human Health Assessment

1. Toxicology Assessment

a. Acute Toxicity

The table below summarizes the toxicity results and categories for technical grade mineral acids. These data are intended for general reference only.

Acute Toxicity

Test	Sulfuric Acid[1]	Sodium Bisulfate[1]	Hydrochloric Acid[1]	Phosphoric Acid[1]
Oral LD_{50} (mg/kg)	II (350)	III (3000)	III (1000)	III (1530)
Dermal LD_{50} (mg/kg)	III (>2000)	III (>10,000)	III (>2000)	III (2740)
Inhalation	I (18 mg/m^3 guinea pig[2])	-	-	-
Eye Irritation	I	I	I	I
Dermal Irritation	I	IV	I	I
Skin Sensitization	NR[3]	NR[3]	NR[3]	NR[3]

1 SAX, N.I., and Lewis, R. J. SR, Dangerous Properties of Industrial Materials, 7th Ed. Van Nostrand Reinhold, New York. 1989 (pg. 2770). The data were waived or not required based on the extensive documentation provided in the literature on this chemical.
2 SAX, N.I., and Lewis, R. J. SR. Dangerous Properties of Industrial Materials, 7th Ed. Van Nostrand Reinhold, New York. 1989 (pg. 3147).
3 Not required based on skin and eye irritation data, i.e. toxicity category I.

b. Other Toxicological Considerations

No additional toxicological studies are required for sulfuric acid, hydrochloric acid and phosphoric acid based on their current use patterns and their corrosiveness as shown in the acute studies for dermal and eye irritation. Additional toxicology studies are not required for sodium bisulfate based on the current use patterns and the fact that it forms ubiquitous metabolic products, sodium and sulfate, that are of little toxicological concern. This applies only to the technical chemicals and does not apply to end use product data requirements.

2. Exposure Assessment

a. Dietary Exposure

Hydrochloric acid, sodium bisulfate, and phosphoric acid currently have no pesticidal type food uses. Sulfuric acid has the only related food uses. This use involves application to potato vines five or more days prior to harvest to desiccate the vines enhancing maturation of the tubers and making harvesting less difficult. Sulfuric acid is exempt from the requirement of a tolerance for residues when used in accordance with good agricultural practice as a herbicide in the production of garlic and onions and as a potato vine desiccant in the production of potatoes [40 CFR §180.1019]. (It should be noted that currently there are no registered products for uses of sulfuric acid on garlic and onions.) Sulfuric acid is rapidly degraded in the environment to yield sulfate ion, which is then available for uptake by plants usually in the form of ammonium, calcium, potassium, and sodium sulfate (sulfate salts). The exemption was based on the expectation that sulfuric acid *per se* would not be found in raw agricultural commodities

and that the levels of sulfate salts resulting from the use of sulfuric acid are of no toxicological concern. The sulfate salts are also generally recognized as safe (GRAS) under 21 CFR §184.1143, §184.1230, §184.1643, and §186.1797, respectively. Furthermore, calcium sulfate and sulfuric acid are often present in phosphorous-containing fertilizers as a result of the use of sulfuric acid in generating wet-process phosphoric acid. There are no human dietary concerns associated with these chemicals.

b. Occupational and Residential

Hydrogen chloride and phosphoric acid are used mainly as antimicrobials to sanitize food and dairy processing plants. For these sites, the concentrations of the active ingredient in the various formulations range from 0.1% to 27.6% hydrogen chloride or 0.1% to 75.5% phosphoric acid. The methods of application include wipe-on surface treatments, spray, and circulate-in-place (CIP) treatments. Contact time can be 1 to 15 minutes.

Sodium bisulfate is supplied as a solid/liquid concentrate for indoor residential use as a disinfectant.

Sulfuric acid (9.5%) is also used to sanitize milk lines and food processing surfaces by CIP and wipe-on treatments as described for the two acids above. This use is followed by a chlorinated alkaline cleaner.

Concentrated sulfuric acid (93%) is a Restricted Use Pesticide (RUP) applied by trained applicators to desiccate mainly white potato vines. This preharvest application "sets" the potatoes and facilitates harvesting. It is applied by special ground boom type equipment by certified applicators on potato fields five days prior to harvest. If necessary the application can be repeated.

There is a potential for post-application dermal and inhalation exposure when the technical active ingredients hydrogen chloride, phosphoric acid, sodium bisulfate or sulfuric acid are used as antimicrobials. However, this exposure is very low since only dilute solutions are used on treated surfaces. Sodium bisulfate is considered toxicity category III (dermal) at 60-70% ai. While the oral and dermal LD_{50}s for hydrogen chloride and phosphoric acid place them in toxicity category III, they are considered toxicity category I for dermal and eye irritation. Since they are applied at low concentrations both mixer/loader/applicator exposure and post-application worker exposure are likely to be negligible. On the basis of these uses and toxicology categories, additional mixer/loader/applicator exposure and post-application worker exposure data for these technical active ingredients for these sites are not required for reregistration eligibility.

Sulfuric acid (93%), when used as a potato vine desiccant, has a potential for dermal and inhalation exposure to mixer/loader/applicators both during and after application. This is a toxicity category I chemical for dermal and eye irritation. Species specific response can result in inhalation toxicity category I or II classification from studies in guinea pigs and rats, respectively. The current label allows for post-application reentry of workers when wearing

appropriate personal protective clothing and equipment (PPE). Otherwise post-application reentry is not permitted for 5 days. The posting of notices when fields are treated is required. It is feasible that initial post-application exposure to workers reentering potato fields can result in severe irritation to mucous membranes and skin. Considering the toxicity category I for dermal irritation and inhalation for concentrated sulfuric acid, the Agency must know on what basis the registrant established the 5 day reentry interval. The registrant must provide data or a rationale for the 5 days currently specified on the label versus a longer reentry interval. In the interim, the Agency requires that workers should not be allowed to reenter treated fields until 5 days have elapsed following treatment with this product. In addition to providing a rationale for the 5 day interval, the labels must be updated to reflect adequate personal protective clothing and equipment for mixer/loader/ applicator and post-application workers as required by the Worker Protection Standards. No further worker exposure data are required for reregistration eligibility, at this time.

3. Risk Assessment

There are no human dietary concerns associated with these chemicals. There is a potential for human exposure to sodium bisulfate, hydrogen chloride, phosphoric acid or sulfuric acid when these chemicals are used as antimicrobials. On the other hand, concentrated sulfuric acid, when used as a potato vine desiccant, results in a high potential for occupational exposure from the treated foliage. The Agency requires that an adequate rationale be provided concerning the 5 day reentry interval into the potato fields. In the interim, The Agency requires that no one be allowed to reenter a treated field, without PPE, until 5 days have elapsed following treatment with this product. Lastly, the labels must be updated to reflect adequate personal protective clothing and equipment as required by the Worker Protection Standards.

B. Environmental Assessment

The fate of acids in the environment is readily predictable using a knowledge of basic chemistry. Similarly, the effect on living organisms of the pH changes caused by these mineral acids can be deduced without requiring actual non-target species testing. Using commonly available sources of information to assess appropriate protection of the environment, the Agency has determined that all but one of the currently-registered uses of the mineral acids are eligible for reregistration. The use of concentrated sulfuric acid on potato vines as a desiccant exceeds the Agency's level of concern for terrestrial species. Since the Agency is not aware of any acceptable methods to mitigate this risk, this use is not eligible for reregistration, at this time.

1. Environmental Fate

In general, these acids will dissociate and release hydrogen ions in the environment, thus increasing the pH. The extent and duration of this increased pH will depend on the amount of neutralizing ions present, the buffering capacity, and the amount of dilution possible.

Terrestrial Fate

Hydrogen Chloride

Hydrochloric acid is a solution of hydrogen chloride gas in water. In water there occurs a complete dissociation of hydrochloric acid to hydronium and chloride ions. The hydronium ion will lower the soil pH, the extent depending upon the buffering capacity of the soil. Chloride ion is a natural component of soils, therefore in the absence of copious amounts of concentrated hydrochloric acid the effect of either ion would be minimal. Neither hydronium nor chloride ions undergo complex transformations which might affect their ultimate impact on the environment.

Phosphoric Acid

Phosphoric acid in water is also strongly acidic. Although, in addition to a variety of indoor uses, phosphoric acid is used in industrial water cooling systems and swimming pool water systems, no significant exposure to terrestrial organisms is expected.

Sodium Bisulfate

Sodium bisulfate in water is strongly acidic. However, because of the limited indoor use of this chemical, environmental exposure is not expected.

Sulfuric Acid

Sulfuric acid is the largest volume chemical produced in the United States and serves mainly non-pesticidal purposes. Sulfuric acid in water dissociates to hydronium and sulfate ions. The effects on the environment of these ions resulting from the anticipated concentrations due to the potato vine desiccant use are moderated by natural means. There is no potential for either ion to be significantly accumulated by the biota.

2. Ecological Effects

a. Ecological Effects Data

Adequate information is available to predict the effect of these acids on living organisms.

For All Mineral Acids and All Uses EXCEPT the Potato Vine Desiccant Use of Sulfuric Acid

The following four studies would normally be required for all of the mineral acids to provide data for labeling statements concerning non-target species:

71-1(a): acute avian oral, quail/duck (TGAI)
71-2(b): acute avian diet, duck (TGAI)
72-1(c): acute fish toxicity/rainbow trout (TGAI)
72-2(a): acute aquatic invertebrate toxicity (TGAI)

Since there is sufficient information regarding the toxic and corrosive nature of the mineral acids all avian and aquatic studies have been waived for these uses.

Sulfuric Acid Potato Vine Desiccant Use

The following six studies would normally be required for the sulfuric acid potato vine desiccant use to provide data for a risk assessment and labeling:

71-1(a): acute avian oral, quail/duck (TGAI)
71-2(a): acute avian diet, quail (TGAI)
71-2(b): acute avian diet, duck (TGAI)
72-1(a): acute fish toxicity/bluegill sunfish (TGAI)
72-1(c): acute fish toxicity/rainbow trout (TGAI)
72-2(a): acute aquatic invertebrate toxicity (TGAI)

Since there is sufficient information regarding the toxic and corrosive nature of sulfuric acid, all data requirements have been waived.

In lieu of Agency guideline quality submitted data on this product, the following information was used to support the ecological effects risk assessment.

(1) Avian Effects

Information on another pesticide documented the potential for adverse effects from acids on avian species. One study was submitted to EPA showing that birds sprayed directly in field pens with both dilute ($\approx$2.1 Molar solution) and undiluted ($\approx$7.03 Molar solution) forms of Enquik (N-TAC, Sulfuric Acid, Monourea adduct) exhibited dermal toxicity effects to areas that were not covered by feathers. Specifically, the eyes and feet were burned by the sulfuric acid released. The birds also showed a significant increase in hemorrhagic enteritis (a severe irritation of the gastrointestinal tract). Another pen study showed dermal toxicity effects to birds after varying reentry times following spraying on alfalfa with dilute Enquick.

(2) Aquatic Effects

Since all of the mineral acids pose a potential hazard to the aquatic environment not because of inherent toxicity but instead due to their ability to change the pH of receiving waters the following discussion, excerpted from: USEPA, 1976, Quality Criteria for Water, pages 178-181, deals with pH and its potential hazard to aquatic organisms. This section also notes safe pH ranges:

"pH" is a measure of the hydrogen ion activity in a water sample. It is mathematically related to hydrogen ion activity according to the expression: $pH = -\log_{10} [H^+]$, where $[H^+]$ is the concentration of the hydrogen ion.

The pH is an important factor in the chemical and biological systems of natural waters. The degree of dissociation of weak acids or bases is affected by changes in pH. This effect is important because the toxicity of many compounds is affected by the degree of dissociation. For example, rapid increases in pH can cause increased NH_3 concentrations which are toxic.

A review of the effects of pH on freshwater fish has been published by the European Inland Fisheries Advisory Commission (EIFAC,1969). The Commission concluded:

> There is no definite pH range within which a fishery is unharmed and outside which it is damaged, but rather, there is a gradual deterioration as the pH values are further removed from the normal range. The pH range which is not directly lethal to fish is 5-9; however, the toxicity of several common pollutants is markedly affected by pH changes within this range, and increasing acidity or alkalinity may make these poisons more toxic. Also, an acid discharge may liberate sufficient CO_2 from bicarbonate in the water either to be directly toxic, or to cause the pH range 5-6 to become lethal.

Based on present evidence, a pH range of 6.5 to 9.0 appears to provide adequate protection for the life of freshwater fish and bottom dwelling invertebrate fish food organisms. Outside of this range, fish may suffer adverse physiological effects increasing in severity as the degree of deviation increases until lethal levels are reached.

For open ocean waters where the depth is substantially greater than the euphotic zone, the pH should not be changed more than 0.2 units from the naturally occurring variation or in any case outside the range of 6.5 to 8.5. For shallow, highly productive coastal and estuarine areas where naturally occurring pH variations approach the lethal limits for some species, changes in pH should be avoided but in any case should not exceed the limits established for fresh water, i.e., pH of 6.5 to 9.0.

b. Ecological Effects Risk Assessment

For All Mineral Acids and All Uses **EXCEPT** the Potato Vine Desiccant Use of Sulfuric Acid

There is sufficient information regarding the toxic and corrosive nature of the mineral acids. Avian species are at risk from direct exposure to mineral acids and such exposure must be avoided. The major potential aquatic hazard of mineral acids lies in their ability to change pH of receiving waters. Sufficient exposure to mineral acids to significantly change the pH is harmful to aquatic species and such exposure must be avoided. Similarly, any such terrestrial or aquatic exposure may be harmful to endangered species.

Sulfuric Acid Potato Vine Desiccant Use

Since there is sufficient information regarding the toxic and corrosive nature of sulfuric acid, all data requirements have been waived. The studies submitted to EPA for Enquik (N-TAC, sulfuric acid, Monourea adduct) demonstrated the potential for adverse avian effects as documented above. Since the concentration of sulfuric acid produced by Enquik (dilute ≈ 2.1, undiluted $\approx$ 7.03 Molar solution) is much less than the 93% used as a potato desiccant (≈ 9.48 Molar solution), use of 93% sulfuric acid as a potato vine desiccant exceeds the Agency's level of concern for terrestrial wildlife.

Precautionary Labelling:

Manufacturing Use for All Mineral Acids and Phosphoric Acid for Use in Industrial Water Cooling Tower Systems

This pesticide is toxic to wildlife. "Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."

Hydrogen Chloride and Phosphoric Acid for Use in Swimming Pools

This pesticide is toxic to wildlife. Do not contaminate water when disposing of equipment wash water or rinsate.

Indoor Uses for All Mineral Acids

Effluent Discharge Labeling Statements

All manufacturing-use or end-use products that may be contained in an effluent discharged to the waters of the United States or municipal sewer systems must bear the following revised effluent discharge labeling statement.

"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."

All affected products distributed or sold by registrants and distributors (supplemental registrants) must bear the above labeling by October 1, 1995. All products distributed or sold by persons other than registrants or supplemental registrants after October 1, 1997 must bear the correct labeling. Refer to PR Notice 93-10 or 40 CFR 152.46(a)(1) for additional information.

Data Requirements:

There are no outstanding data requirements to support the present uses of the mineral acids (hydrogen chloride, sulfuric acid, phosphoric acid, sodium bisulfate).

Conclusion:

For All Mineral Acids and All Uses **EXCEPT** the Potato Vine Desiccant Use of Sulfuric Acid

The potential risks of the mineral acids to non-target organisms will be mitigated through labelling statements.

Sulfuric Acid Potato Vine Desiccant Use

Use of 93% sulfuric acid as a potato vine desiccant is expected to pose significant hazard to terrestrial wildlife. Since the risk is focused in the treated field and occurs during treatment and continues for a number of hours after treatment, there are no known practical mitigation measures. Therefore, this use exceeds the Agency's level of concern for risk to terrestrial wildlife.

Endangered Species

At the present time, the Agency is working with the U.S. Fish and Wildlife Service and other federal and state agencies to develop a program to avoid jeopardizing the continued existence of listed species by the use of pesticides. When the Endangered Species Protection Program is implemented and subsequent guidance is given, endangered species labeling amendments may be required on affected end-use products. Labeling statements for end-use products will likely refer users to county specific bulletins specifying detailed limitations on use to protect endangered species.

IV. RISK MANAGEMENT AND REREGISTRATION DECISION

A. Determination of Eligibility

Section 4(g)(2)(A) of FIFRA calls for the Agency to determine, after submission of adequate data concerning an active ingredient, whether products containing the active ingredients are eligible for reregistration. The Agency has identified the generic (i.e. active ingredient specific) data required to support reregistration of products containing mineral acid active ingredients. The Agency has completed its review of these generic data, and has determined that the data are sufficient to support reregistration of all products containing mineral acids except for the use of sulfuric acid on potato vines. Appendix B identifies the generic data requirements that the Agency reviewed as part of its determination of reregistration eligibility of mineral acids, and lists the submitted studies that the Agency found acceptable.

The Agency is not able to determine, at this time, if the use of sulfuric acid as applied to potato vines is eligible for reregistration. The Agency is concerned about the risk to terrestrial wildlife and is not aware of any acceptable methods to mitigate the risk. In order to determine its eligibility, the Agency will be assessing the benefits of sulfuric acid for this use. Once this is done, the Agency will make a finding of whether this use is eligible for reregistration and whether any further regulatory action is required.

Even though the use on potato vines is not eligible at this time, if the registrants of these sulfuric acid products still wish to support them for reregistration, they must comply with all appropriate product specific labeling and data requirements including data or an adequate rationale in support of the 5-day post-harvest re-entry interval.

The Agency made its reregistration eligibility determination based upon the target data base required for reregistration, the current guidelines for conducting acceptable studies to generate such data and the data identified in Appendix B. Although the Agency has found that most uses of mineral acids are eligible for reregistration, it should be understood that the Agency may take appropriate regulatory action, and/or require the

submission of additional data to support the registration of products containing mineral acids if new information comes to the Agency's attention or if the data requirements for registration (or the guidelines for generating such data) change.

1. Eligibility Decision

Based on the reviews of the generic data for the active ingredients mineral acids, the Agency has sufficient information on the health effects of mineral acids and on its potential for causing adverse effects in fish and wildlife and the environment. Therefore, the Agency concludes that products, labeled and used as specified in this Reregistration Eligibility Decision, containing mineral acids for all uses except for the use of sulfuric acid on potato vines, are eligible for reregistration.

2. Eligible and Ineligible Uses

The Agency has determined that all uses of mineral acids except for the use of sulfuric acid on potato vines, are eligible for reregistration.

B. Regulatory Position

The following is a summary of the regulatory positions and rationales for mineral acids. Where labeling revisions are imposed, specific language is set forth in Section V of this document.

1. Tolerance Reassessment

Sulfuric acid is exempt from the requirement of a tolerance for residues when used in accordance with good agricultural practice as a herbicide in the production of garlic and onions and as a potato vine desiccant in the production of potatoes [40 CFR §180.1019]. (It should be noted that currently there are no registered products with uses of sulfuric acid on garlic and onions.) Sulfuric acid is rapidly degraded in the environment to yield sulfate ion, which is then available for uptake by plants usually in the form of ammonium, calcium, potassium, and sodium sulfate (sulfate salts). The exemption was based on the expectation that sulfuric acid *per se* would not be found in raw agricultural commodities and that the levels of sulfate salts resulting from the use of sulfuric acid are of no toxicological concern.

2. Restricted Use Classification

Sulfuric acid products to be applied as a desiccant to potato vines are currently Restricted Use Products, i.e. their mixing, loading, and application may only be done by or under the direct supervision of an (EPA) Certified Applicator. This classification was enacted historically to protect human health.

V. ACTIONS REQUIRED BY REGISTRANTS

This section specifies the data requirements and responses necessary for the reregistration of both manufacturing-use and end-use products.

A. Manufacturing-Use Products

1. Additional Generic Data Requirements

The generic data base supporting the reregistration of mineral acids for the above eligible uses has been reviewed and determined to be substantially complete except for one requirement for sulfuric acid. Registrants of the products which contain sulfuric acid for use on potato vines are required to provide data or a rationale for foliar residue dissipation corresponding to series 132-1(a).

2. Labeling Requirements for Manufacturing-Use Products

Effluent Discharge Labeling Statements

All manufacturing-use or end-use products that may be contained in an effluent discharged to the waters of the United States or municipal sewer systems must bear the following revised effluent discharge labeling statement.

"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA."

All affected products distributed or sold by registrants and distributors (supplemental registrants) must bear the above labeling by October 1, 1995. All products distributed or sold by persons other than registrants or supplemental registrants after October 1, 1997 must bear the correct labeling. Refer to PR Notice 93-10 or 40 CFR 152.46(a)(1) for additional information.

B. End-Use Products

1. Additional Product-Specific Data Requirements

Section 4(g)(2)B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticide after a determination of eligibility has been made. The product specific data requirements are listed in Appendix G, the Product Specific Data Call-In Notice.

Registrants must review previous data submissions to ensure that they meet current EPA acceptance criteria (Appendix F; Attachment E) and if not, commit to conduct new studies. If a registrant believes that previously submitted data meet current testing standards, then study MRID numbers should be cited according to the instructions in the Requirement Status and Registrants Response Form provided for each product.

2. Labeling Requirements for End-Use Products

The labels and labeling of all products must comply with EPA's current regulations and requirements as specified in 40 CFR §156.10.

In the course of the reregistration of phosphoric acid and hydrogen chloride, the Agency has become aware of a number of products that make claims regarding disinfection of critical items (surgical instruments) and semi-critical items (catheters, endoscopes, respiratory apparatus, etc.). [See discussion in Section 2.C. "Regulatory History" above and Appendix D "FDA/EPA Memorandum of Understanding"].

The Agency believes that, in fact, these products are general purpose disinfectants and therefore, these claims for disinfection of critical items and semi-critical items must be removed from the labels.

Worker Protection Standard

Any product whose labeling reasonably permits use in the production of an agricultural plant on any farm, forest, nursery, or greenhouse must comply with the labeling requirements of PR Notice 93-7, "Labeling Revisions Required by the Worker Protection Standard (WPS), and PR Notice 9311, "Supplemental Guidance for PR Notice 93-7, which reflect the requirements of EPA' s labeling regulations for worker protection statements (40 CFR part 156, subpart K). These labeling revisions are necessary to implement the Worker Protection Standard for Agricultural Pesticides (40 CFR part 170) and must be completed in accordance with, and within the deadlines specified in, PR Notices 93-7 and 93-11. Unless otherwise specifically directed in this RED, all statements required by PR Notices

93-7 and 93-11 are to be on the product label exactly as instructed in those notices.

After April 21, 1994, except as otherwise provided in PR Notices 93-7 and 93-11, all products within the scope of those notices must bear WPS PR Notice complying labeling when they are distributed or sold by the primary registrant or any supplementally registered distributor.

After October 23, 1995, except as otherwise provided in PR Notices 93-7 and 93-11, all products within the scope of those notices must bear WPS PR Notice complying labeling when they are distributed or sold by any person.

Effluent Discharge Labeling Statements

Refer to subsection A. above for labeling requirements for effluent discharge.

C. Existing Stocks

Registrants may generally distribute and sell products bearing old labels/labeling for 26 months from the date of the issuance of this RED. Persons other than the registrant may generally distribute or sell such products for 50 months from the date of the issuance of this RED. However, existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors. Refer to "Existing Stocks of Pesticide Products; State of Policy"; Federal Register, Volume 56, No. 123, June 26, 1991.

The Agency has determined that registrants may distribute and sell mineral acid products bearing old labels/labeling for 26 months from the date of issuance of this RED. Persons other than the registrant may distribute or sell such products for 50 months from the date of the issuance of this RED.

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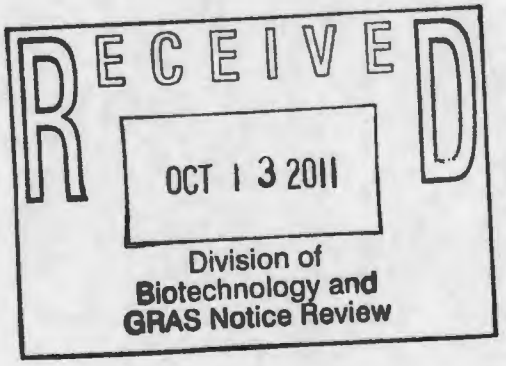
--------	"Summary of Toxicity Data: Experimental Herbicide Formulation". ES Unilab Research, Inc. [unpublished study], 1981.
--------	Trent, L.; Hestand, R.; Carter, C. "Toxicity of Sulfuric Acid to Aquatic Plants and Organisms." Journal of Aquatic Plant Management, 1978.

Appendix II: Proof of Antimicrobial Use in Meat and Poultry Processing

Advanced Food Technologies, LLC

11230 Magnolia Glen
Shreveport, LA 71106

October 12, 2011



Via Federal Express

Antonia Mattia, Ph.D.
Office of Food Additive Safety
Division of Biotechnology and GRAS Notice Review (HFS-255)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740

Re: GRAS Notification for Sulfuric Acid and Sodium Sulfate Blend Used as an Anti-Microbial in Meat and Poultry Processing

Dear Dr. Mattia:

By this letter, Advanced Food Technologies, LLC ("AFT") is submitting four copies of a GRAS Notification for its AFTEC 3000 product which is a blended combination product containing sulfuric acid and sodium sulfate. AFT has determined that AFTEC 3000 is generally recognized as safe ("GRAS") for use as an anti-microbial agent for the treatment of meat and poultry to reduce levels of micro-organisms (bactericidal) and to prevent microbial growth (bacteria static). The product is intended for use on the surface of meat or poultry and can be delivered via spray, wash or dip.

AFTEC 3000 and its proposed uses are exempt from the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act because AFT has determined through scientific procedures that such use is GRAS. AFT's GRAS determination is likewise supported by the fact that the Food and Drug Administration ("FDA") has previously affirmed each of the constituent components (i.e., sulfuric acid and sodium sulfate); various blends containing at least one of AFTEC 3000's included constituent components (i.e., sulfuric acid / ammonium sulfate / copper sulfate blends); and a variety of other acids (i.e., acetic acid, phosphoric acid) as GRAS.

AFT is including a fourth copy of the submission for FDA to share with the U.S. Department of Agriculture ("USDA") since the proposed use occurs within USDA regulated facilities.

Advanced Food Technologies, LLC

11230 Magnolia Glen
Shreveport, LA 71106

October 12, 2011

Via Federal Express

Antonia Mattia, Ph.D.
Office of Food Additive Safety
Division of Biotechnology and GRAS Notice
Review (HFS-255)
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5100 Paint Branch Parkway
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AFTEC 3000 and its proposed uses are exempt from the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act because AFT has determined through scientific procedures that such use is GRAS. AFT's GRAS determination is likewise supported by the fact that the Food and Drug Administration ("FDA") has previously affirmed each of the constituent components (i.e., sulfuric acid and sodium sulfate); various blends containing at least one of AFTEC 3000's included constituent components (i.e., sulfuric acid / ammonium sulfate / copper sulfate blends); and a variety of other acids (i.e., acetic acid, phosphoric acid) as GRAS.

AFT is including a fourth copy of the submission for FDA to share with the U.S. Department of Agriculture ("USDA") since the proposed use occurs within USDA regulated facilities.

If for any reason the agency has any questions or requires any additional information to aid its review of AFT's conclusion, please contact us at the address listed above or our counsel, Robert G. Hibbert (202-778-9315) at your earliest convenience.

Sincerely,

(b) (6)

Stephen Mixon
Director of Operations

Enclosures

cc: Judith L. Kidwell, FDA
Susan Carlson, FDA
John Hicks, FSIS
Robert G. Hibbert, K&L Gates

GRAS NOTIFICATION

FOR SULFURIC ACID

AND

SODIUM SULFATE BLEND

SUBMITTED BY

ADVANCED FOOD TECHNOLOGIES, LLC

GRAS NOTIFICATION FOR A SULFURIC ACID AND SODIUM SULFATE BLEND FOR USE AS AN ACIDIFIER OR ANTI-MICROBIAL ON MEAT AND POULTRY

1 GRAS NOTIFICATION FOR A SULFURIC ACID AND SODIUM SULFATE BLEND FOR USE AS AN ACIDIFIER OR ANTI-MICROBIAL AGENT FOR MEAT AND POULTRY

Advanced Food Technologies, LLC ("AFT") manufactures a blended product containing sulfuric acid and sodium sulfate for use as an acidifier or anti-microbial agent for meat or poultry and is intended to be delivered via spray, wash or dip. The trade name of the product is AFTEC 3000 but it will also be known as AFT Clear 3000 (hereafter, referred to as "AFTEC 3000").

AFTEC 3000 is intended for use as an acidifier or anti-microbial agent for meat and poultry to reduce levels of micro-organisms (bactericidal) and to prevent microbial growth (bacteria static). Chemically equivalent to Sodium Bisulfate in Solution, the product contains both sulfuric acid and sodium sulfate in blend. The included sodium sulfate, which is a natural conjugate salt of sulfuric acid, serves as a buffering agent to the sulfuric acid. Diluted to a targeted pH of 1.0-2.2 for use in the form of a spray, wash or dip; AFTEC 3000 kills microbes via the low pH effect.

AFT's product is manufactured using food grade raw materials recognized under the Food Chemical Code ("FCC") in accordance with the U.S. Food and Drug Administration's ("FDA") current Good Manufacturing Practices ("cGMPs") by Harcros Chemicals Inc. in Vicksburg, Mississippi.

Pursuant to the regulatory and scientific procedures set forth in the Proposed Rule "Substances Generally Recognized as Safe," 62 Fed. Reg. 18937 (April 17, 1997) (proposed 21 C.F.R. § 170.36) ("GRAS Proposed Rule"), AFT has determined, through scientific procedures, that AFTEC 3000 is GRAS for use as an antimicrobial agent in levels not to exceed cGMPs and is therefore exempt from the requirement for premarket approval. General and specific information identifying and characterizing AFTEC 3000, its applicable conditions for use, and other supporting information provide the basis for AFT's GRAS determination.

There are several sulfuric acid blends in use today in meat and poultry plants in the U.S. They are used for their anti-microbial properties. Examples of such blends include 1) sodium acid sulfate or sodium bisulfate (used as an acidifier for meat and poultry, and used in bread making); 2) sulfuric acid + ammonium sulfate + copper sulfate (used as an acidifier for poultry scalders, pickers, NY rinse and post-chill treatment); and 3) sulfuric acid + citric acid + phosphoric acid (used as a poultry application including on-line reprocessing, chill treatment and post chill applications). In all of these products, the sulfuric acid is the main active anti-microbial component. The other components serve simply as buffering agents to allow for the safe handling of the sulfuric acid.

Likewise, several additional acids are currently used individually or in combination as blends with meat and poultry in the U.S including among others, acetic acid, phosphoric acid, sulfuric acid, hydrochloric acid, citric acid, sodium bisulfate (sodium acid sulfate) and hypochlorous acid (from chlorine + water). These acids are designated as acidifiers or anti-microbial agents, and are identified in the U.S. Department of Agriculture ("USDA") Food Safety and Inspection Service's ("FSIS") Directive 7120.1. *See* "Safe and Suitable Ingredients Used in the Production of Meat, Poultry, and Egg Products," FSIS Directive 7120.1, Revision 7 (July 1, 2011).

The material and data included in this submission clearly shows the safety of AFTEC 3000 for use as an acidifier or anti-microbial agent with meat or poultry. As outlined in the prior Table of Contents, Section 1 provides general information identifying and characterizing AFTEC 3000, its applicable conditions for use, and the basis for AFT's GRAS determination. Section 2 describes the AFTEC 3000 product and its chemical solution. Section 3 discusses the manufacturing process to make AFTEC 3000. Section 4 discusses the product's formulation. Section 5 includes a discussion of application and Section 6 is the Safety Evaluation. Lists of attachments and references also accompany the notification.

1.1 Name and Address of Notifier

NOTIFIER

Advanced Food Technologies, LLC
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Shreveport, LA 71106
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1.2 Common or Usual Name of Substance

AFT produces a sulfuric acid and sodium sulfate blend for use as an acidifier or anti-microbial on meat or poultry. The trade name of the product is AFTEC 3000. The product is also known as AFT Clear 3000.

1.3 Applicable Conditions of Use

AFTEC 3000 is intended for use as an acidifier or anti-microbial to reduce the level of micro-organisms (bactericidal) and to prevent microbial growth (bacteria static) on meat and poultry. It is delivered in the form of a spray, wash, or dip. Equivalent to Sodium Bisulfate in Solution, AFTEC 3000 contains both sulfuric acid and sodium sulfate, and kills microbes by the low pH effect. *See* Growth Factors for Selected Bacteria, Pathogen Modeling Program Online, USDA Agricultural Research Service (Last accessed on October 11, 2011) (Attachment 1).[1]

When used as a spray, wash, or dip, the microbial reduction has a temporary effect and the chemical solution quickly drips off, evaporates, or otherwise leaves no significant chemical residue and has no lasting technical effect.

1.3.1 Substances Used In

AFTEC 3000 is intended for use directly on meat and poultry surfaces. This includes whole carcasses, parts, trimmings, organs and cut meats.

1.3.2 Levels of Use

AFTEC 3000 is diluted with water to a pH level that is suitable for the intended purposes stated above. For proper anti-microbial efficacy this is usually a pH range of 1.0 – 2.0 which amounts to a 1/25 – 1/500 volumetric dilution of the product with water respectively. The most common working target is pH 1.5 or a 1/100 dilution. A table comparing pH levels by volumetric dilution rate and product weight is included below.

Dilution (v/v)	pH	Wt% AFTEC	Wt% H_2SO_4	Wt% Na_2SO_4
1/25	1.0	5.44	2.12	0.27
1/100	1.5	1.38	0.54	0.07
1/500	2.0	0.28	0.11	0.01

1.3.3 Purposes

AFTEC 3000 is intended for use as an acidifier or anti-microbial to reduce the level of micro-organisms (bactericidal) and to prevent microbial growth (bacteria static) on meat and poultry. Examples of proposed applications are described below:

Beef Processing - In the multi-hurdle approach in beef processing, AFTEC 3000 can be used in several processing steps to reduce microbial contamination, including hide wash, eviscerated carcass wash, parts wash, on primals and cut meats, and on trimmings prior to grinding.

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[1] Available at http://pmp.arserrc.gov/PMPOnline/References/GrowthFactors.aspx

Poultry Processing - In the multi-hurdle approach in poultry processing, AFTEC 3000 can be used in several processing steps to reduce microbial contamination, including with scalders, pickers, New York rinse, on-line reprocessing, chillers, post-chill dips, on parts such as organs and feet (paws), and trimmings prior to grinding.

1.4 Basis for AFT's GRAS Determination

Pursuant to the GRAS Proposed Rule, AFT has determined, through scientific procedures that the combination of sulfuric acid and sodium sulfate is GRAS for use as an antimicrobial agent in levels not to exceed current good manufacturing practices. The safety of AFTEC 3000 is supported by the fact that the blended product readily dissolves in aqueous media into the same constituent ions as the components that are used for its manufacture. Individually, each of the constituent components has been affirmed as GRAS by the FDA. For the reasons explained below, AFTEC 3000 is affirmed to be GRAS for use as an acidifier and by extension, a processing aid.

FDA states in its 2009 and 2011 letters to AFT with respect to sulfuric acid:

> "Sulfuric acid (CAS Reg. No. 7664-93-9) is listed under 21 C.F.R. § 184.1095 for use as a pH control agent and as a processing aid."

FDA states with respect to sodium sulfate:

> "Sodium sulfate (CAS Reg. No 7727-73-3) is listed for use as a direct food additive under §172.615 where it is permitted for use as a masticatory substance, stabilizer, thickener or gelling agent. It is also listed for use as a secondary direct additive under §173.310 as permitted for use as a boiler water additive or processing aid."

FDA also noted:

> "Sodium sulfate is the soluble salt formed by sulfuric acid and sodium hydroxide. Both sulfuric acid (21 CFR § 184.1095) and sodium hydroxide (21 CFR § 184.1763) are generally recognized as safe (GRAS) substances that completely ionize in water to form sodium sulfate ions and more water. Therefore, sodium sulfate is also GRAS and can be used as a processing aid in accordance with 21 CFR § 174.5(d)(1), which authorizes GRAS substances for use as indirect additives. The only limitation on the use levels of either of these compounds would be based on good manufacturing practice (GMP) in accordance with 21 CFR §148.1(b)(1), which means using the minimum amount to accomplish the intended technical effect."

See FDA Letters to Stephen Mixon, Director of Operations, Advanced Food Technologies, LLC (July 1, 2009; August 30, 2011) (Attachment 2). *See also* 21 C.F.R. § 172.5 (In the context of direct food additives, the term "good manufacturing practice" means using the minimum amount to accomplish the intended technical effect.)

Furthermore, FSIS has previously recognized the use of AFTEC 3000 in meats and poultry in different capacities.[2] Equivalent to sodium bisulfate, FSIS Directive 7120.1 allows for the product's use 1) as a pH control agent and processing aid in water used in meat and poultry processing at levels "sufficient for purpose;" 2) as a pH control agent in meat and poultry soups at levels not to exceed 0.8 % of the product formulation; and 3) for addition to sauces used as separable components in the formulation of various meat products at levels sufficient for such purposes (citations to GRAS Notice GRN No. 3 included). *See* FSIS Directive 7120.1. Since FSIS requires assurances of the GRAS status of an ingredient before accepting the suitability of the use, the above-listed uses can be considered GRAS.

Based on FDA's various GRAS determinations with respect to sulfuric acid, sodium sulfate and the various blends referenced above; it is appropriate to assume by extension that the FDA also recognizes the GRAS status of AFTEC 3000 in all foods, including meat and poultry, as a pH adjuster and processing aid. Furthermore, FSIS has already accepted the GRAS status of these ingredients in combination as a pH adjuster, and considering that but for notation of the impact on microbes, there is no substantive difference in the use and ingredient levels of such products and AFTEC 3000, it is appropriate to conclude that AFTEC 3000 is equally safe for use as a pH adjuster and as an antimicrobial agent.

Since the use range, method of application, and targeted products for AFTEC 3000 when used as an antimicrobial will be the same as the use range, method of application, and targeted products for AFTEC 3000 when used as a pH adjuster, there are no novel safety issues presented that have not previously been addressed. Accordingly, AFTEC 3000 is GRAS when used as an antimicrobial agent in meat and poultry.

When used as an anti-microbial agent, AFTEC also satisfies the regulatory requirements for being a processing aid under 21 C.F.R. § 101.100(a)(3)(ii)(c). Processing aids are substances that are added to a food for their technical or functional effect in the processing but are present in the finished food at insignificant levels and do not have any technical or functional effect in that food. AFTEC 3000 clearly meets this definition.

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[2] FSIS confirmed by letter that AFTEC 3000 is the same as sodium bisulfate, and thus, would be considered to have the same regulatory status as sodium bisulfate. *See* FSIS Letter to Advanced Food Technologies, LLC (November 4, 2008) (Attachment 3).

1.5 Availability of Information for FDA Review

The data and information that are the basis for AFT's GRAS determination are available for the FDA's review, and copies will be sent to FDA upon request. Requests for copies and arrangements for review of materials cited herein may be directed to:

Robert G. Hibbert, Esq.
Gary L. Yingling, Esq.
K&L Gates LLP
1601 K Street, NW
Washington, DC 20006-1600

2.0 DETAILED INFORMATION ABOUT THE IDENTITY OF THE NOTIFIED AFTEC 3000 PRODUCT

2.1 Identity

AFTEC 3000 is a blend of sulfuric acid and sodium sulfate in purified water.

Sulfuric Acid (CAS #7664-93-9) is commonly used as an acidifier. It is a strong mineral acid that fully dissociates in water ($H_2SO_4 \Rightarrow 2H^+$ and $SO_4^=$). While it therefore could be an ideal anti-microbial solution, its corrosive nature makes sulfuric acid difficult to handle in its concentrated form. Even when diluted, sulfuric acid can cause organoleptic damage to treated meats. However, when blended with its conjugated base salt (any sulfate) or even a weaker organic acid (like citric acid) the equilibrium solution is significantly less corrosive to skin and meat tissue.

Sulfuric acid is GRAS and is included by FDA in the regulations. *See* 21 C.F.R. § 184.1095. As per the regulations, it meets the specifications for the FCC. It is intended for use as a pH control agent and as a processing aid. The regulations set maximum use levels for the chemical.

The USDA also recognizes sulfuric acid as an approved single ingredient acidifier and processing aid at levels sufficient for certain defined purposes when used in accordance with cGMPs. *See* FSIS Directive 7120.1. FSIS also allows for sulfuric acid to be blended with other acids or sulfates to create a safer acidifier. Such combinations include:

- Sulfuric acid, ammonium sulfate, copper sulfate, and water for use in poultry processing;
- An aqueous solution of sulfuric acid, citric acid, and phosphoric acid to adjust the pH in poultry chill water and processing water in meat and poultry plants; and
- An aqueous solution of sodium bisulfate and sulfuric acid as a pH control agent in poultry processing water to a pH of 1.0-6.0.

See FSIS Directive 7120.1.

Sodium Sulfate (CAS #7757-82-6) serves strictly as a buffering salt for the sulfuric acid in this case. It has no anti-microbial properties of its own. Sodium sulfate is a salt formed from the reaction of two GRAS substances (sulfuric acid and sodium hydroxide) and it fully dissociates in water ($Na_2SO_4 \Rightarrow 2Na^+$ and $SO_4^=$). It is GRAS and permitted for use as a direct food additive under 21 C.F.R. § 172.615 as a masticatory substance, stabilizer, thickener or gelling agent. It is also listed for use as a secondary direct additive under 21 C.F.R. § 173.310 as a boiler water additive or processing aid. The desired buffering capability can be achieved at 1:5 – 1:10 ratios with sulfuric acid (that is 10-20% of the amount of sulfuric acid by weight in the finished blend).

2.2 Characteristic Properties

AFTEC 3000 Characteristic Properties	
Appearance	It is a clear, colorless to light amber liquid.
Odor	None to slightly acidic.
Solubility	Very soluble in water.
pH (1:100 v/v dilution with neutral water)	1.4 – 1.6
Specific Gravity @25°C	1.38

2.3 Quantitative Composition

AFTEC 3000 is the product of blending the following materials to achieve the targeted levels.

Material	Target Wt%	Spec Range Wt%
Sulfuric Acid (H_2SO_4)	39.0	38.5 – 39.5
Sodium Sulfate (Na_2SO_4)	5.0	4.5 – 5.5
Water (H_2O)	56.0	55.0 – 57.0
Total	100.0%	

3 MANUFACTURING PROCESS

3.1 Overview

The sulfuric acid and sodium sulfate blend described in this dossier is produced by Harcros Chemicals Inc. at its Vicksburg, Mississippi facility for AFT in accordance with industry recognized cGMPs.

Batch sheets are used for the recording of raw material and production information for every batch produced. Every batch is assigned a unique lot number for identification / traceability purposes.

The production process uses 98% sulfuric acid that is diluted with water to make a 41% sulfuric acid solution in a dedicated blend / storage tank. Sodium sulfate (anhydrous) crystals are added to the tank containing the diluted acid solution while the tank is circulated (pumps are used to draw the solution from the bottom and re-circulated through the top). The tank in which the blend is produced is thoroughly mixed and samples are taken for Quality Control ("QC") purposes to ensure that product specifications are met. The product is then filtered and transferred through dedicated pipelines to designated packaging areas for packaging into bulk (tank trailer), IBC (totes) and drums.

Typical batch amounts for 1,000gals of AFTEC 3000 are below. Note the final water content comes from the 41% sulfuric acid.

Material	Amount in lbs	Wt%	Wt% in Final Product
41% Sulfuric Acid	10,925	95.0	39.0% sulfuric acid
Sodium Sulfate	575	5.0	5.0% sodium sulfate
Water			56.0% water

3.2 Raw Materials

The raw materials used for the blending of the product are suited for the intended use thus supporting the safety of the finished product. The raw materials meet predefined quality standards that are controlled by the Quality Assurance Department of AFT ("QA Dept.") and the contracted Chemical Blender. The raw materials used for the formulation meet food grade standards (i.e., FCC standards) and are sourced from NorFalco (98% sulfuric acid) and Saltex (sodium sulfate, anhydrous). Water used is from the local municipal/city water source.

Raw material lot numbers are recorded for every batch produced and every lot is inspected / received based on purchase order specifications and certificates of analysis.

3.3 Quality Control of Finished Product

The specifications for the AFTEC 3000 product are outlined below:

Material	Target Wt%	Spec Range Wt%
Sulfuric Acid (H_2SO_4)	39.0	38.5 – 39.5
Sodium Sulfate (Na_2SO_4)	5.0	4.5 – 5.5
Water (H_2O)	56.0	55.0 – 57.0
Total	100.0%	

The wt% target and specification ranges are based on the material amounts (weights) recorded on the batch sheet. Samples are collected from every batch produced and are tested for appearance, specific gravity and pH to meet the following specifications.

Specifications for Sample Testing	
Appearance	Clear, colorless to slight amber liquid. Free of particulates.
Specific Gravity @ 25°C	1.37 – 1.39
pH (1/100 v/v dilution)	1.4 – 1.6

Final product batch samples are retained for 1 year.

4 COMPOSITION AND SPECIFICATIONS

4.1 Formulation

The common starting materials for the blended product are sulfuric acid, sodium sulfate and water. All of the raw materials used are of food grade quality and satisfy FCC standards.

Apart from these materials, the blended product may also contain substances commonly found and tested for in food grade raw materials. Such substances generally consist of sulfate impurities of iron and magnesium, and are recognized under FCC specifications and testing requirements.

4.2 General Production Controls and Specifications (Good Manufacturing Practices)

4.2.1. Technical Measures

AFTEC 3000 is prepared, preserved and stored in such a way that contamination is avoided. This is achieved by dedicated production equipment, piping and tanks; trained production personnel, documented standard operating procedures; and the preparation and maintenance of batch records. The product is clearly labeled and stored in dedicated tanks and shipping containers. Only new drums and totes are used for packaging. Bulk trailer shipments are made in rubber-lined trailers that undergo food grade washouts, washout certificates are issued before loading, and such certificates are maintained by the manufacturer.

The manufacturing of product and the cleaning of the equipment are laid down in Quality Assurance documents and strictly followed by trained personnel.

4.2.2. Control Measures

The raw materials used to produce the product are appropriate for the intended use thus supporting the safety of the finished product. The raw materials meet predefined quality standards that are controlled by the AFT's QA Dept. and the chemical blender. The raw materials are of food grade quality and comply with FCC specifications.

The finished product is subjected to extensive product and quality controls as outlined in Section 3 above.

5 APPLICATION

5.1 Mode of Action

As is well recognized by scientific experts in the industry, most microorganisms cannot tolerate a high or low pH environment.[3] Any pH environment below a 4.0 pH begins to kill the organisms. The efficacy of any antimicrobial kill step is a function of concentration and time (K = C x T). Since pH is a negative log scale of the concentration of the Hydrogen ion (H+), the lower the pH, the higher the concentration and the faster the kill step.

The function of the AFTEC 3000 product is to provide significant microbial reductions on the surfaces of poultry and meat without imparting any lasting technical effects or chemical residues, or causing any organoleptic damage to the meats. AFTEC 3000 performs this function by utilizing a strong inorganic acid, sulfuric acid, to provide the microbe killing Hydrogen ions (H+) and a buffering agent, sodium sulfate, to minimize any damage to the treated meats, plant workers, and USDA inspection personnel.

5.2 Application

AFTEC 3000 is intended for use directly on meat and poultry surfaces as a spray, wash, or dip in order to temporarily reduce the level of microbes on the food surface. This would include whole carcasses, parts, trim, organs and cut meats. As a spray, wash, or dip the microbial reduction is a temporary effect and the chemical solution will drip off, evaporate, or otherwise leave no significant chemical residue and have no lasting technical effect. Examples of such application are included below.

AFT submitted a request to FSIS for waiver of the regulatory requirements under 9 C.F.R. § 381.91(b) (1) for permission to conduct an on-line reprocessing ("OLR") trial to determine whether AFTEC 3000 is an effective antimicrobial agent in an OLR application which FSIS granted. In support of its request, AFT provided FSIS with data from seven studies conducted at the University of Georgia showing that AFTEC 3000 is an effective antimicrobial agent when used as a dip or spray for the reduction of microbes on broiler chickens. FSIS granted AFT's waiver request. *See* Summary and Report from Background Studies with Poultry to Support Waiver Request (Log #10-OLR-0514-N-A (March 15, 2010) (Attachment 4).

5.2.1. FSIS Approved Poultry On-Line Reprocessing

The approved poultry on-line reprocessing study was conducted at Tyson Foods, Inc.'s Forest, Mississippi facility ("Tyson's Study"). Over a 10 day period, 400 carcasses were identified as being either visually uncontaminated or visually contaminated. 100 carcasses (10 per day per condition) were rinsed before and after the OLR. The pH of the AFTEC solution applied to the carcasses was measured before and after each trial. The protocol provided for an operating range

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[3] *See* Growth Factors for Selected Bacteria. Attachment 1.

from 1.4-2.2 pH. Samples pulled during the tests ranged from 1.5-1.9 pH. *See* Analysis of On-Line Reprocessing Results with AFTEC 3000 as an Antimicrobial Agent on Poultry (2010 - 2011) (Attachment 5).

The APC and *E. coli* count numbers showed 90 and 85 percent statistically significant reductions from pre-OLR to post-OLR, respectively. *Salmonella* spp. showed a low positive incidence pre and post-OLR, so even though there was a 50 percent reduction in positive incidence post-OLR compared to pre-OLR, the reduction could not be shown to be statistically significant. The study authors concluded that AFTEC 3000 is an effective antimicrobial agent in the OLR.

Upon completion, the results of the Tyson's Study were submitted to FSIS in support of a request to expand the waiver to two additional facilities, which was approved by FSIS. *See* FSIS Letter Granting AFT Permission to Conduct Additional In-Plant Trials (March 8, 2011) (Attachment 6). Based upon its review of the results of the Tyson's Study, FSIS granted the waiver request concluding that the data:

> ... showed that the number of aerobic plate count (APC) bacterial, *Escherichia coli*, and *Salmonella* positive samples was statistically reduced after passage through the AFTECT 3000 (AFT Clear 3000) OLR system. The data showed that there was no statistical microbiological difference between carcasses marked visibly clean and those marked visibly contaminated after decontamination with the AFTECT 3000 (AFT Clear 3000) OLR treatment.

Under the FSIS granted waiver, AFT was given permission to conduct testing at two additional facilities. This included a second in-plant trial at Pilgrim's Pride (establishment # P6638) in Enterprise, Alabama and a third in-plant trial at Gold'n Plump (establishment # P322) in Cold Springs, Minnesota. Testing at the two facilities is ongoing and data will be provided to FSIS upon completion of the studies. While AFT continues to conduct studies to validate the application methods of AFTEC 3000, initial data indicates that the solution is clearly effective as an antimicrobial agent in poultry processing.

5.2.2. Secondary Beef Processing Study at Oklahoma State University

The Oklahoma State University ("OSU") study was conducted in two phases to address blade tenderized beef contamination issues for the potential to carry surface contamination (i.e., *E. coli* O157:H7) into the interior of steak cuts, and whether this presents a potential health risk to consumers. *See* Summary and Technical Report of Integral Antimicrobial Solution Application on the Ross Blender Tenderizer, Phase 1 and Phase 2 Results Report (April 2, 2011) (Attachment 7).

Phase 1 determined the effectiveness of AFTEC 3000 at a pH of 1.0 as an antimicrobial on beef surfaces inoculated with *E. coli* O157:H7 through quantification of survivors to determine reduction of initial population on the surface. *E. coli* O157:H7 colonies were measured at 1 hour, 1 day, 7 days, and 14 days, and the data was plotted on a chart depicting the comparative difference in amount of pathogens (log reduction (cfu/cm^2)) in the treated sample as compared to the control (rinsed with water). In phase 1, lean beef wafers sprayed with AFTEC were observed

to have a 1.19 log reduction (cfu/cm^2) of *E. coli* O157:H7 after 1 hour. Data collected after 1 day, 7 days, and 14 days revealed a slight increase in comparative difference of amount of *E. coli* between the control and samples treated with AFTEC 3000, consistent with expectations. The comparative difference in amounts of pathogens between the control and treated samples after the initial kill step persisted over time. AFT believes this is because a reduced amount of pathogens likely remained after the treatment of the sample with AFTEC 3000 generating a lower amount of pathogens as compared to the control whose colonies flourished and multiplied. As with all pH treated meats however, the pH quickly increased back to a neutral pH providing an environment more suitable for all microorganisms, including spoilage bacteria and pathogens, to grow. This also occurred with samples treated with AFTEC 3000. The data showed only a slight increase in the comparative difference of *E. coli* colonies after 1 day, 7 days, and 14 days demonstrating that AFTEC 3000 had an immediate, non-continuous impact on *E. coli* growth.

Phase 2 used surface-inoculated beef whole muscle cuts followed by spray treatment of AFTEC 3000 at a pH of 1.0. Blade tenderization was performed immediately to determine the level of microbial entry after interventions are applied compared to an untreated control. Researchers looked for recovery of internalized *E. coli*, which was expected to be proportional to the reduction of *E. coli* O157:H7 on the surface (i.e., the greater the reduction on the surface, the less likely one will recover it from internalized sections after blade tenderization). That is, a sufficiently high population on the surface was needed to observe translocation to internal sections. For the samples inoculated with *E. coli* O157:H7, spray-treated with AFTEC 3000 and then blade-tenderized during Phase 2, only 8 core sections tested positive for *E. coli* O157:H7 as compared to 15 core control sections.

The study report concludes that the use of antimicrobial spray interventions prior to blade tenderization (i.e., integral solution intervention) has an immediate, non-continuous impact on reducing the population of *E. coli* O157:H7 thus lowering levels than those that exist prior to spray treatment, and therefore, reduces the likelihood of translocation to beef internal sections concomitant with lower surface populations.

There were a total of 14 different anti-microbial chemicals or brands tested in this OSU study. All were applied in the same equipment at constant flows and pressures at manufacturer's recommended dosage rates. AFTEC 3000 consistently performed in the top quartile of microbial performance.

5.3 Use Levels

When using a low pH spray or dip in a meat or poultry plant,, the generally accepted operating range of the dilute solution is 1.0-2.2 pH, with a target of 1.3-1.8 pH for the best combination of efficacy and cost.

As supported by the results for each of the product categories, AFT concludes that it is suitable to use AFTEC 3000 in beef and poultry products as an antimicrobial agent at levels necessary to achieve targeted pH ranges. Typical pH ranges will vary between 1.0-2.2 pH and will vary according to instrumentation and application as validated by individual processors for specific product.

5.4 Residues in the Final Food

AFTEC 3000 has been tested as a spray and as a dip in various meat and poultry plants and in controlled plant-equivalent laboratory settings at several major universities.

5.4.1. Antimicrobial Beef Study

In a study conducted at Kansas State University ("KSU"), researchers examined whether AFTEC 3000 has a continuing technical effect after the product is spray-treated and then stored. *See* Summary and KSU Study Report on Anti-Microbial Treatment of Beef Trimmings (October 13, 2009) (Attachment 8). The study conducted a sensory evaluation comparing a control to ground beef manufactured using beef trimmings treated with AFTEC at 10, 20, and 30 second time intervals in triangle tests using a trained sensory panel. No differences between the treated samples and the control were reported.

The study also examined the shelf life of treated products. Samples were evaluated daily for visual color and microbiological testing for total aerobic plate count. No differences in color stability were observed between treated samples versus the control. No significant differences in aerobic plate counts were reported between treated and control ground beef samples.

The study report states:

> There was no long term residual effect on the color, shelf life, or microbiological quality of ground beef manufactured from the treated trimmings versus the control. In addition, no statistical differences in residual levels of sodium sulfate or sulfuric acid were reported in ground beef treated with the *AFTEC* solution versus control samples.

Therefore, any AFTEC 3000 that remains on the product is insignificant, and after the initial antimicrobial impact during the spray treatment, AFTEC 3000 has no technical or functional effect in the beef product. Accordingly, this study demonstrated that AFTEC 3000 may properly be qualified as a processing aid based on the KSU data indicating that only de minimis residues are found on the final product and that AFTEC 3000 does not have a long-term residual effect on the color, shelf life, or microbiological quality of ground beef.

5.4.2. Poultry Studies

In support of its initial waiver request referenced above, AFT provided FSIS with a University of Georgia study that examined the potential chemical residue of AFTEC 3000 as an antimicrobial spray solution. *See* Summary of Studies Conducted to Support FSIS Waiver Request, Pages 5-7 (Attachment 4). In that study, 5 control carcasses were sprayed with tap water, and 5 test samples were sprayed with AFTEC 3000 for 5 seconds and allowed to drip for 2 minutes. The meat from each part (i.e., skin, fat) was compared (control versus test) for each chemical component (sulfur or sodium) using statistical analysis of variation or ANOVA. From a review of the data, it was determined that the study demonstrated no statistical difference between samples treated with tap water (controls) and samples treated with AFTEC 3000 in a spray

solution. Therefore, the study concluded that no chemical residue exists on the skin, fat, or meat of chicken carcasses treated using AFTEC 3000.

In the same FSIS waiver request, AFT included another University of Georgia study that evaluated the ability of AFTEC 3000 to impact aerobic plate counts or psychrotrophic plate counts (spoilage bacteria) after treatment and storage of poultry. *See* Summary of Studies Conducted to Support FSIS Waiver Request, Pages 7-9 (Attachment 4). In this study, eighty carcasses were collected before entering the on-line reprocessing system in a commercial poultry operation. The carcasses were then transported to the Poultry Research Center at the University of Georgia where they were separated into groups of 10 each and subjected to the following:

1) 10 carcasses were tested prior to any treatment as controls

2) 10 carcasses were sprayed with tap water using a commercial sprayer and allowed to hang on the line for 1 minute, then placed for 1 hour in tap water with ice and aeration, then sampled as chill controls

3) 10 carcasses were sprayed with tap water using a commercial sprayer and allowed to hang on the line for 1 minute, then sampled as spray controls

4) 10 carcasses were sprayed with tap water using a commercial sprayer and allowed to hang on the line for 1 minute, then placed for 1 hour in tap water with ice and aeration, then held for 24 hours at 4°C, and sampled as chill 24 h controls

5) 10 carcasses were sprayed with tap water using a commercial sprayer and allowed to hang on the line for 1 minute, then placed for 1 hour in tap water with ice and aeration, then held for 48 hours at 4°C, and sampled as chill 48 h controls

6) 10 carcasses were sprayed with AFTEC 3000 at a pH of 1.5 and allowed to sit for no longer than 1 minute, then sampled

7) 10 carcasses were sprayed with AFTEC 3000 at a pH of 1.5 and allowed to sit for no longer than 1 minute, then placed for 1 hour in tap water with ice and aeration, then held for 24 hours at 4°C, and sampled (AFTEC Chill 24 hr)

8) 10 carcasses were sprayed with AFTEC 3000 at a pH of 1.5 and allowed to sit for no longer than 1 minute, then placed for 1 hour in tap water with ice and aeration, then held for 48 hours at 4°C, and sampled (AFTEC Chill 48 hr)

9) Carcasses were sampled using 400 mL of 0.1% buffered peptone water with neutralizer

10) Rinses were diluted and plated onto 2 sets of Petrifilm Aerobic Count Plates

11) 1 set of plates was incubated at 37°C for 48 hours and counted (APC Counts)

12) 1 set of plates was incubated at 7°C for 10 days and counted (psychrotrophic plate counts)

13) Means for each group were graphed and compared using the ANOVA procedure of SAS

The study data indicates that even though AFTEC 3000 was sprayed onto the carcasses, no additional reductions in aerobic plate counts ("APC") or psychrotrophic plate counts (spoilage bacteria-PPC) were observed when compared to the other groups (except the original control / untreated group). Moreover, and most importantly, APC and PPC bacteria counts on carcasses sprayed with AFTEC 3000 and tested immediately, after 24 hours of storage or after 48 hours of storage, were not significantly different. This means that no residual effect on spoilage bacteria occurred for carcasses treated with AFTEC 3000 during storage.

Based on the test data obtained, AFTEC 3000 clearly satisfies the regulatory requirements for being considered a processing aid under 21 C.F.R. § 101.100(a)(3)(ii)(c). Despite being sprayed on beef and poultry for its antimicrobial effects during processing, it is present in the finished product only at insignificant levels and does not have any technical or functional effect on that food.

AFT intends to label the AFTEC 3000 product with the following ingredient declaration: "purified water, sulfuric acid, sodium sulfate." Since it will be used as a processing aid, manufacturers using AFTEC 3000 will not be required to include AFTEC 3000 on their labels. Despite their usage of AFTEC 3000, the finished meat and poultry products will comply with all applicable FSIS labeling requirements.

6. SAFETY EVALUATION

6.1 Safe Acid Chemistry

AFTEC 3000 is an example of 'Safe Acid' technology in which a strong acid is buffered by a weaker acid or conjugate base salt. AFTEC 3000 is made by blending a solution of water, sodium sulfate (salt) and sulfuric acid. The sodium sulfate acts as a conjugate base when mixed in a water solution with sulfuric acid. Sodium sulfate is the salt formed from the reaction of a strong acid (sulfuric acid) and strong base (sodium hydroxide). Salts from the reaction of a strong acid and strong base generally are neutral in pH (7), and can be used as a buffering compound for the strong acid. There are many other examples of 'Safe Acids' that work according to this same chemical principal that are used daily in various food and water applications.

The AFTEC 3000 product is made by blending a solution of sulfuric acid (H2SO4), water (H2O), and sodium sulfate (Na2SO4). The resulting solution contains sulfuric acid, sodium sulfate, sodium bisulfate, water, sodium ions (Na^+), hydrogen ions (H^+), hydrogen sulfate ions (HSO_4^-) and sulfate ions ($SO_4^=$). These are the exact same ionic species that are formed when Sodium bisulfate (NaHSO4) is dissolved in water (H2O).

6.2 FSIS & FDA Recognition of Safety

There are three listings in FSIS Directive 7120.1 for sodium bisulfate. These include 1) for use as a pH control agent and processing aid in water used in meat and poultry processing at levels "sufficient for purpose"; 2) pH control agent in meat and poultry soups at levels not to exceed 0.8 % of product formulation; and 3) for addition to sauces used as separable components in the formulation of various meat products at levels sufficient for purpose.

In addition, FDA GRAS Notice GRN No. 0003 discusses the use of sodium bisulfate as a leavening agent in cake mixes at a level of 1 to 10 grams sodium bisulfate per 1000 grams of total mix (0.1% to 1.0% by weight). *See* Sodium Bisulfate GRAS Notice, GRN No. 3 (June 5, 1998).

Sulfuric acid as a single ingredient product is affirmed as GRAS in 21C.F.R. § 184.1095. The ingredient is used as a pH control agent and processing aid. "Current good manufacturing practice results in a maximum level, as served, of 0.014 percent for alcoholic beverages...and 0.003 percent for cheeses..."

Sodium sulfate is listed for use as a direct food additive under 21 C.F.R. §172.615 where it is permitted for use as a masticatory substance, stabilizer, thickener or gelling agent. It is also permitted for use as a secondary direct additive under 21 C.F.R. §173.310 as permitted for use as a boiler water additive used in the preparation of steam that will contact food.

6.3 Residual Studies

As an anti-microbial, AFTEC 3000 is intended for use directly on meat and poultry as a spray, wash, or dip in order to temporarily reduce the level of microbes on a food's surface. This includes whole carcasses, parts, trimmings, organs and cut meats. Whether delivered as a spray, wash, or dip; the microbial reduction is a temporary effect and the chemical solution drips off, evaporates, or otherwise leaves no significant chemical residue and has no lasting technical effect.

During the Kansas State University study referenced above, AFTEC 3000 was applied as an anti-microbial wash to beef trimmings prior to grinding. The study demonstrated significant microbial reduction without any chemical residues or lasting technical effects. *See* Attachment 7. Specifically, the report states:

> There was no long term residual effect on the color, shelf life, or microbiological quality of ground beef manufactured from the treated trimmings versus the control. In addition, no statistical differences in residual levels of sodium sulfate or sulfuric acid were reported in ground beef treated with the *AFTEC* solution versus control samples.

Likewise, the numerous studies on poultry conducted by Dr. Scott Russell at the University of Georgia produced similar results. (Attachment 4). In those studies, significant microbial reductions were achieved with no chemical residue remaining on the skin, fat, or meat of the chicken carcasses treated with AFT's AFTEC 3000 product. Also, no lasting technical effects were measured or observed.

When used as an anti-microbial agent, AFTEC 3000 satisfies the regulatory requirements for a processing aid as defined under 21 C.F.R. § 101.100(a)(3)(ii)(c). The regulations define processing aids as substances that are added to a food for their technical or functional effect in the processing but are present in the finished food at insignificant levels and do not have any technical or functional effect in that food.

Therefore, when used as an anti-microbial agent, foods treated with an AFTEC 3000 spray, wash, or dip would have insignificant levels of the product or its components in the final food. These levels, if any, would be far less than those levels already generally recognized as safe in foods for the components sulfuric acid, sodium sulfate, and sodium bisulfate. Thus, it can be concluded that there are no novel safety issues presented and no risk to the population consuming food that has been treated with AFTEC 3000. Accordingly, AFTEC 3000 should be recognized as GRAS when used as an antimicrobial agent in meat and poultry processing.

7. LIST OF ATTACHMENTS

Attachment 1: Growth Factors for Selected Bacteria, Pathogen Modeling Program Online, USDA Agricultural Research Service (Last accessed on October 11, 2011)

Attachment 2: FDA letters to AFT from 2009 and 2011 regarding the GRAS status of AFTEC 3000 and its components for use as a pH control agent and processing aid on meat and poultry.

Attachment 3: USDA FSIS letter to AFT dated Nov 4, 2008 confirming that AFT Clear 3000 (AFTEC 3000) is equivalent to sodium bisulfate and permitted by FSIS to be used as a pH control agent in water used in meat and poultry processing sufficient for the purpose.

Attachment 4: Summary and Report from Background Studies with Poultry to Support Waiver Request (Log #10-OLR-0514-N-A) (March 15, 2010)

Attachment 5: Analysis of On-Line Reprocessing Results with AFTEC 3000 as an Antimicrobial Agent on Poultry (2010 - 2011)

Attachment 6: USDA FSIS letter to AFT dated March 8, 2011 granting permission to conduct the second and third in-plant trials of AFTEC 3000 in the On-Line Reprocessing application in poultry slaughter plants.

Attachment 7: Summary and Technical Report of Integral Antimicrobial Solution Application on the Ross Blender Tenderizer, Phase 1 and Phase 2 Results Report (April 2, 2011)

Attachment 8: Summary and KSU Study Report on Anti-Microbial Treatment of Beef Trimmings (October 13, 2009)

8. LIST OF REFERENCES

1. Safe and Suitable Ingredients Used in the Production of Meat, Poultry, and Egg Products, USDA FSIS Directive 7120.1, Revision 7 (July 1, 2011).

2. 21 C.F.R. § 184.1095 (Lists sulfuric acid as GRAS for use as a pH control agent and processing aid.)

3. 21 C.F.R. § 172.615 (Supports the use of sodium sulfate as a direct food additive for use as a masticatory substance, stabilizer, thickener or gelling agent.)

4. 21 C.F.R. § 173.310 (Lists Sodium Sulfate as a secondary direct additive permitted for use as a boiler water additive and processing aid for steam generation for direct contact with food.)

5. 21 C.F.R. § 174.5(d)(1) (Authorizes GRAS substances for use as indirect additives.)

6. 21 C.F.R. § 172.5(a)(1) (In the context of direct food additives, the term "good manufacturing practice" means using the minimum amount to accomplish the intended technical effect.)

7. Sodium Bisulfate GRAS Notice, GRN No. 3 (June 5, 1998) (The GRAS notice allowing for the use of sodium bisulfate as a pH control agent and use as a leavening agent for cake mixes.)

8. 21 C.F.R. § 101.100(a)(3)(ii)(c) (Defines a processing aid as substances that are added to a food for their technical or functional effect in the processing, but are present in the finished food at insignificant levels and do not have any technical or functional effect in that food.)

Attachment 1

United States Department of Agriculture
Agricultural Research Service

ERRC
EASTERN REGIONAL RESEARCH CENTER

Pathogen Modeling Program (PMP) Online

- PMP Home
- PMP Online
  - About PMP
  - Tutorial
  - Frequently Asked Questions
  - ***References***
    - pH of Selected Foods
    - Water Activity in Food
    - ***Growth Factors***
    - Model Development
    - Publications List

You are here: PMP Home / PMP Online / References / Growth Factors

Growth Factors For Selected Bacteria

ORGANISM	TEMP °C[a]	pH[a]	a_W[a]
Salmonella spp.	5.2 / 35-43 / 46.2	3.8 / 7.0-7.5 / 9.5	0.94 / 0.99 / >0.99
Clostridium botulinum			
A & B	10 - 50	4.7 - 9	>0.93
nonproteolytic B	5 - ?	-[b]	NR[c]
E	3.3 - 15-30	-[b]	>0.965
F	4 - ?	-[b]	NR[c]
Staphylococcus aureus	7 / 37 / 48	4.0 / 6.0-7.0 / 10	0.83(0.9) / 0.98 / >0.99
Campylobacter jejuni	32 / 42-43 / 45	4.9 / 6.5-7.5 / ca9	>0.987 / 0.997 / -
Yersinia enterocolitica	-1.3 / 25-37 / 42	4.2 / 7.2 / 9.6	- / - / 5% NaCl
Listeria monocytogenes	-0.4 / 37 / 45	4.39 / 7.0 / 9.4	0.92 / - / -
Vibrio cholerae O1	10 / 37 / 43	5.0 / 7.6 / 9.6	0.970 / 0.984 / 0.998
V. cholerae non-O1	-[b]	-[b]	-[b]
Vibrio parahaemolyticus	5 / 37 / 43	4.8 / 7.8-8.6 / 11	0.940 / 0.981 / 0.996
Clostridium perfringens	4 / 43-47 / 50	5.5-5.8 / 7.2 / 8.0-9.0	0.97 / 0.95-0.96 / 0.93
Bacillus cereus	4 / 30-40 / 55	5.0 / 6.0-7.0 / 8.8	0.93 / - / -
Escherichia coli	ca7-8 / 35-40 / ca44-46	4.4 / 6-7 / 9.0	0.95 / 0.995 / -
Shigella sonnei	6.1 / - / 47.1	4.9 / - / 9.34	- / - / 5.18% NaCl
Shigella flexneri	7.9 / - / 45.2	5.0 / - / 9.19	- / - / 3.78% NaCl

a. minimum / optimum / maximum values.
b. The value, though unreported, is probably close to other species of the genus.
c. NR denotes that no reported value could be found, but for most vegetative cells, an a_W of >0.95 would be expected.

Values taken from:

ICMSF(1996) Microorganisms in Foods 5: Characteristics of Microbial Pathogens, Roberts, T. A., Baird-Parker, A. C. and Tompkin, R. B. (eds.), Blackie Academic & Professional, London [ISBN 0 412 47350 X]

Microbial Survival in the Environment, E. Mitscherlich and E.H. Marth (eds.), Springer-Verlag, Berlin and Heidelberg, 1984. [ISBN 3-540-13726-2 Springer-Verlag, Berlin, New York, Tokyo] [ISBN 0-387-13726-2 Springer-Verlag, Heidelberg, Berlin, Tokyo].

Attachment 2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

July 1, 2009

Stephen Mixon
Director of Operations
Advanced Food Technologies, LLC
3614 Windhill Ln.
Montgomery, TX 77356

Dear Mr. Mixon:

This responds to your inquiry dated May12, 2009, requesting information on the regulatory status of your product (Trade name: AFTEC 3000) for use as a pH control agent or processing aid in water used on poultry, red meat and seafood processing. Specifically, you provided the information on the chemical composition, proposed applications, and use levels for your product.

In general, FDA does not "certify" products or packaging for use in contact with food. Instead the agency authorizes the use of specific chemicals in the production of such food-contact articles or products. FDA's primary method for authorizing such uses is the food contact notification (FCN) process. Please note, however, that only the listed manufacturer/supplier and their customers are authorized to market the product of an effective FCN. Previously, FDA published regulations for such uses in Parts 174 to 189 of Title 21 of the U.S. Code of Federal Regulations (CFR). These regulations prescribe safe conditions of use for components of food contact materials. Therefore, in order to market your product(s) in the U.S., all the chemical components would have to be authorized for their intended use or we would suggest that you should submit a food contact notification following FDA's current guidelines for the preparation and submission of a food contact notification which may be accessed on the internet at:
http://www.cfsan.fda.gov/~lrd/foodadd.html.

FDA recognizes that opinion letters from the agency can serve as a valuable tool of assurance for consumers and for this reason we are available to assist the manufacturer in producing compliant products by providing interpretations of food additive regulations or policy. Moreover, it is the manufacturer's responsibility to ensure that their products comply with all appropriate regulations whenever the products enter into interstate commerce in the U.S.

By way of background, when reviewing a product to determine compliance in the 21CFR, you should consider each regulation to be composed of three parts: the *identity* of the substance,

specifications including purity or physical properties, and *limitations* on the conditions of intended use. In order for your products to be suitable for use in contact with food, each chemical component must comply with all three criteria.

For your product you have correctly identified the components of your product and their corresponding applicable regulations. Sulfuric acid (CAS Reg. No. 7664-93-9) as listed under 21 CFR §184.1095 is permitted for use as a pH control agent and as a processing aid.

Sodium sulfate (CAS Reg. No 7727-73-3) is listed for use as a direct food additive under §172.615 where it is permitted for use as a masticatory substance, stabilizer, thickener or gelling agent. It is also listed for use as a secondary direct additive under §173.310 as permitted for use as a boiler water additive or processing aid. Sodium sulfate (Anhydrous) (CAS Reg. No 7757-82-6) is listed under §186.1797 as permitted for use as an antimicrobial agent. Also note, sodium sulfate is the soluble salt formed by sulfuric acid and sodium hydroxide. Both sulfuric acid (21 CFR §184.1095) and sodium hydroxide (21 CFR §184.1763) are generally recognized as safe (GRAS) substances that completely ionize in water to form sodium sulfate ions and more water. Therefore, sodium sulfate is also GRAS and can be used as a processing aid in accordance with 21 CFR 174.5(d)(1), which authorizes GRAS substances for use as indirect additives. The only limitation on the use levels of either of these compounds would be based good manufacturing practice (GMP) in accordance with 21 CFR §148.1(b)(1), which means using the minimum amount to accomplish the intended technical effect.

I hope that this information has been responsive to your questions regarding your product. If you have any further questions concerning this matter, please do not hesitate to contact us.

Sincerely,

Vivian Gilliam
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
Center for Food Safety
And Applied Nutrition

cc: HFA-224 HFS-200 HFS-275
Letter No. 93332
R/D:HFS-275:VGilliam:06/20/09
INIT:EMachuga:HFS-275:07/01/09
F/T:HFS-275:VGilliam:

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

August 30th, 2011

Stephen Mixon
Director of Operations
Advanced Food Technologies, LLC
3614 Windhill Ln.
Montgomery, TX 77356

Dear Mr. Mixon:

This is to clarify our response of June 24, 2009 to your inquiry dated May12, 2009, requesting information on the regulatory status of your product (Trade name: AFTEC 3000) for use as a pH control agent or processing aid in water used on poultry, red meat and seafood processing. Specifically, you provided the information on the chemical composition, proposed applications, and use levels for your product.

In general, FDA does not "certify" products or packaging for use in contact with food. Instead the agency authorizes the use of specific chemicals in the production of such food-contact articles or products. FDA's primary method for authorizing such uses is the food contact notification (**FCN**) process. Please note, however, that only the listed manufacturer/supplier and their customers are authorized to market the product of an effective FCN. Previously, FDA published regulations for such uses in Parts 174 to 189 of Title 21 of the U.S. Code of Federal Regulations (CFR). These regulations prescribe safe conditions of use for components of food contact materials. Therefore, in order to market your product(s) in the U.S., all the chemical components would have to be authorized for their intended use or we would suggest that you should submit a food contact notification following FDA's current guidelines for the preparation and submission of a food contact notification which may be accessed on the internet at:
http://www.cfsan.fda.gov/~lrd/foodadd.html.

FDA recognizes that opinion letters from the agency can serve as a valuable tool of assurance for consumers and for this reason we are available to assist the manufacturer in producing compliant products by providing interpretations of food additive regulations or policy. Moreover, it is the manufacturer's responsibility to ensure that their products comply with all appropriate regulations whenever the products enter into interstate commerce in the U.S.

By way of background, when reviewing a product to determine compliance in the 21CFR, you should consider each regulation to be composed of three parts: the *identity* of the substance, *specifications* including purity or physical properties, and *limitations* on the conditions of intended use. In order for your products to be suitable for use in contact with food, each chemical component must comply with all three criteria.

Sodium sulfate is the soluble salt formed by sulfuric acid and sodium hydroxide. Both sulfuric acid (21 CFR §184.1095) and sodium hydroxide (21 CFR §184.1763) are generally recognized as safe (GRAS) substances that completely ionize in water to form sodium sulfate ions and more water. Therefore, sodium sulfate is also GRAS and can be used as a processing aid in accordance with 21 CFR 174.5(d)(1), which authorizes GRAS substances for use as indirect additives. The only limitation on the use levels of either of these compounds would be based good manufacturing practice (GMP) in accordance with 21 CFR §148.1(b)(1), which means using the minimum amount to accomplish the intended technical effect. Sodium sulfate would also be considered GRAS for use as a secondary direst additive when used as a pH control agent or processing aid in water used on poultry, red meat and seafood processing.

I hope that this information has been responsive to your questions regarding your product. If you have any further questions concerning this matter, please do not hesitate to contact us.

Sincerely,

(b) (6)

Vivian Gilliam
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
Center for Food Safety
And Applied Nutrition

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

August 30, 2011

Correction Letter

Stephen Mixon
Director of Operations
Advanced Food Technologies, LLC
3614 Windhill Ln.
Montgomery, TX 77356

Dear Mr. Mixon:

This letter is to correct a statement provided in our previous opinion letter. The response letter dated June 24, 2009 provided information that was in error. Specifically, the letter provided incorrect information when it cited the following statement: "Sodium sulfate (Anhydrous) (CAS Reg. No 7757-82-6) is listed under §186.1797 as permitted for use as an antimicrobial agent."

Please note that sodium sulfate (Anhydrous), listed under 21 CFR §186.1797, as permitted for use as a constituent of paper and paperboard and cotton and cotton fabric, only and **not** for use as an antimicrobial agent. I apologize for any inconvenience that this incorrect advice may have caused. I will also send you a revised response letter for your files.

If you have any further questions concerning this matter, please do not hesitate to contact us.

Sincerely,

[redacted]

Vivian Gilliam
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
Center for Food Safety
And Applied Nutrition

Attachment 3

United States Department of Agriculture | Food Safety and Inspection Service | Washington, D.C. 20250

Mr. Dennis Smithyman
President
Advanced Food Technologies, LLC
11230 Magnolia Glen
Shreveport, LA 71106

NOV 0 4 2008

Dear Mr. Smithyman:

This is in response to your October 30, 2008 email (Log number 08-NT-0387-N-A) requesting a letter from the Food Safety and Inspection Service (FSIS) stating that AFT Clear 3000 is the same as sodium bisulfate and under FSIS Directive 7120.1, "Safe and Suitable Ingredients Used in the Production of Meat and Poultry Products" can be used as an acidifier in meat and poultry plants.

After reviewing your submitted information, FSIS has determined that AFT Clear 3000 is considered the same as sodium acid sulfate (SAS) or sodium bisulfate and, thus, would not be considered new technology. SAS or sodium bisulfate is already permitted by FSIS to be used as a pH control agent (acidifier) in water used in meat and poultry processing sufficient for the purpose.

This letter should not be considered as validation that your process will be effective in any particular FSIS establishment. Your technology, as described in your notification, will need to be factored into an establishment's hazard analysis and, if appropriate, incorporated into its HACCP Plan or SSOP, or other prerequisite program, validated for its application, and verified on an ongoing basis for its effectiveness. If the establishment does not address the effects of using your technology in its hazard analysis, FSIS would be unable to determine that the product processed using your technology is safe, including microbiologically, not adulterated; and therefore, the product would not be eligible to bear the mark of inspection.

If you have any questions, please contact Dr. David Zeitz at (202)690-3556 or david.zeitz@fsis.usda.gov.

Sincerely,

[redacted]

Dr. John Hicks, Director
Risk and Innovations Management Division
Office of Policy and Program Development

FSIS FORM 2620-8 (6/96) EQUAL OPPORTUNITY IN EMPLOYMENT AND SERVICES

Attachment 4

Study title: Background Studies to support request for an in-plant trial of AFTEC 3000 for use in on-line reprocessing of poultry (Log#10-ING-0498-N-A)

Conducted by: Scott M Russell, Ph.D., Professor, Dept. of Poultry Science, University of Georgia

Study dates: March 15, 2010

Objective: to evaluate the efficacy of application of AFTEC 3000 as a means of reducing pathogenic and indicator populations of bacteria on ready-to-cook carcasses. Also, evaluate effect on shelf life, color, and residues.

Methodology: A total of 7 anti-microbial studies (Section IV) were conducted over a 1 year time frame on chicken carcasses. Studies 1 & 3 were in-plant post-chill spray cabinets; study 4 was a lab study for a post-chill dip, while study 2 was an in-plant post-chill dip; Studies 5, 6, and 7 were in-plant pre-chill spray cabinets or dips. All of the tests were conducted with AFTEC 3000 diluted to a pH range between 1.4 and 2.0.

The residual studies (Section III) addressed both chemical residues and evaluation of the ability of AFTEC 3000 to have a residual impact on aerobic plate counts or psychrotrophic plate counts (spoilage bacteria) after treatment and storage of poultry. The chemical residual study compared 5 treated and 5 control carcasses. The skin, meat, and fat of of each carcass was aseptically excised and analyzed for component levels of sulfuric acid and sodium sulfate. A total of 80 carcasses were used for various treatments and controls to determine the effect on psychrotrophic plate counts (PPC) immediately after treatment and after storage for 24 or 48 hours.

Results and discussion: Across the 7 anti-microbial studies, AFTEC 3000 consistently validated statistically significant reductions in overall microbial levels and *Salmonella* spp. Whether as a spray or a dip, AFTEC 3000 usually achieved a greater than 1 log reduction in generic E.coli CFU/ml and a measurable percent reduction in Salmonella incidence if sufficient Salmonella were present pre-treatment in the plant.

In the chemical residue study, 5 carcasses were sprayed with AFTEC 3000 for 5 seconds and allowed to drip for 2 minutes. 5 untreated carcasses were used for control. The means for each part (skin, fat, or meat) were compared (control versus test) for each chemical component (sulfur or sodium) using ANOVA. The study demonstrated no statistical difference between samples treated with tap water (controls) or samples treated with AFTEC 3000 in a spray solution.

In the study on the impact of AFTEC 3000 on psychrotrophic plate counts (spoilage bacteria), there was no residual effect on spoilage bacteria compared with normal water sprays or dips used in the plant after treatment and storage.

Background Studies to support request for an in-plant trial of AFTEC 3000 for use in on-line reprocessing of poultry

(Log#10-OLR-0514-N-A)

March 15, 2010

Respectfully Submitted by: Scott M. Russell, Ph.D. on behalf of
Denny Smithyman, President
Advanced Food Technologies, LLC
11230 Magnolia Glen
Shreveport, LA 71106
(908) 385-7216

Contact Person: Scott M. Russell, Ph.D.
Professor
Department of Poultry Science
Poultry Science Bldg.
The University of Georgia
Athens, GA 30602-2772

Table of Contents

I. Purpose of the research

The purpose of this research was to evaluate the efficacy of application of AFTEC 3000 (AFT Clear 3000) as a means of reducing pathogenic and indicator populations of bacteria on ready-to-cook carcasses. The components of the AFTEC 3000 concentrate are as follows: sulfuric acid (25-35%), sodium sulfate (5-15%), water (50-70%). This concentrate is diluted by mixing with tap water to reach the target levels of pH for each of the applications.

II. Literature Review

Studies have been conducted for the last three decades in an effort to discover means of reducing pathogenic bacterial populations on raw poultry products; however, contamination of raw poultry continues to be a concern for consumers, industry, and regulatory agencies [1]. Addition of chlorine, hydrogen peroxide [1], and antimicrobials such as halogenic compounds, organic acids, and salts [2] to the chiller have been used effectively to reduce microorganisms in the water, but no significant reduction in *Salmonella* has been demonstrated on carcasses. This may be explained because there are numerous areas on the carcass that afford protection for bacteria, such as feather follicles, and cuts or folds in the skin or fat [3,4]. Using electron microscopy, it has been shown that bacteria appear to be entrapped in ridges and crevices, which become more pronounced in the skin and muscle following water immersion [5]. This may make bacteria on carcasses inaccessible to antimicrobial agents.

Because the chiller is a common bath, opportunities exist for *Salmonella* to wash off of one contaminated carcass and to be transported to other uncontaminated carcasses. Lillard [6] reported that populations of aerobic bacteria and Enterobacteriaceae on broiler carcasses were significantly reduced by commercial processing steps, but cross-contamination still occurred. The author found that there was no increase in *Salmonella* prevalence on carcasses at five sampling points from the kill line through the final washer, but a significant increase in *Salmonella* prevalence occurred on carcasses exiting the immersion chiller, indicating that this may be the point of most significant cross-contamination in broiler processing plants [6].

The most commonly used chiller disinfectant in the broiler industry is chlorine. Lillard [7] observed that *Salmonella* Typhimurium, inoculated onto broiler breast skin and treated using 0.5 ppm free residual Cl_2, were not readily accessible to the chlorine and were only reduced by $< 1 \log_{10}$. It is suspected that greater reductions do not occur using chlorine because of the abundance of organic material and nitrogenous compounds associated with chicken carcasses that deactivate

forms of chlorine [8]. In addition, chlorine is coming under increasing scrutiny by European countries and Canada because of the formation of carcinogenic trihalomethane compounds. Hydrogen peroxide has been shown to be effective for eliminating total aerobic bacteria (95-99.5% reduction using 6,600 ppm or higher) and *E. coli* (97 – 99.9% reduction using 5,300 ppm or higher); however, the concentrations required to successfully eliminate these bacterial populations caused the carcasses to become bleached and bloated as the catalase in the blood of the chicken reacted with the H_2O_2 [4]. Ozone has been used successfully to eliminate 99% of the bacteria washed off of carcasses into chiller water as a means of controlling cross-contamination [9].

Numerous trials have indicated that organic acids, such as lactic and acetic acid, can be used in a variety of ways to either decrease or eliminate salmonellae from the carcass and extend shelf-life of processed broilers [10]. However, some chemicals at high concentrations may produce undesirable organoleptic characteristics. Dickens and Whittemore [11] reported that Enterobacteriaceae counts on broiler carcasses were reduced by 0.50, 0.71, and 1.4 $\log_{10}$ when using 0.6% acetic acid (AA), air agitation and 0.6% acetic acid (AGAA), or a paddle chiller with 0.6% acetic acid (PAA), respectively. *Salmonella* prevalence on inoculated carcasses after treatment were 87% for control carcasses, 80% (AA), 53% (AGAA), and 6.7% for the (PAA) treatments [11].

Trisodium phosphate has become popular as a solution approved by USDA-FSIS for disinfecting carcasses as an automated reprocessing method. Lillard [12] evaluated trisodium phosphate for eliminating *Salmonella* from broiler carcasses. The author reported that salmonellae levels were reduced by 2 $\log_{10}$ colony forming units (CFU)/mL rinse. However, use of high levels of phosphates (10%) to wash chickens during processing creates an enormous amount of phosphorous in the waste-stream that must be eliminated prior to release to the environment.

The scalder is the first common bath during poultry processing. As such, it represents the first location where pathogenic bacteria from one carcass may wash off and contaminate many other carcasses. This is of concern because of the USDA HACCP/Pathogen Reduction Final Rule [13] which uses *Salmonella* prevalence as a regulatory criterion, as opposed to the number of *Salmonella* cells per carcass. Therefore, any operation that presents an opportunity for one *Salmonella* positive carcass to cause many other *Salmonella* negative carcasses to become positive is of great concern to the industry. A major problem exists in that the chemicals listed above are not used in the scalder because they are inappropriate for use in high temperature, high organic load situations.

AFTEC 3000 (AFT Clear 3000) has been a USDA-FSIS approved acidifier since November 2008. This product has been tested and used in numerous poultry plants over the past year in scalders, pre- and post-evis sprays, pre- and post-chill dips and sprays and is used to acidify chillers.

AFTEC 3000 has been shown that it can be used in scalder water to eliminate bacterial populations. It is not affected by organic material as are the oxidants (Cl, ClO_2, ozone, acidulated sodium chlorite, and H_2O_2), it is not affected by scalder temperatures (130 – 135ºF), and does not cause organoleptic defects.

AFTEC 3000 has been used and tested in poultry plants in pre- and post-evis spray cabinets at a pH range of 1.5 to 2.0. Carcass dips are also conducted in this 1.5-2.0 pH range. Significant microbial reductions are achieved with no organoleptic damage to carcasses and no off-gassing of the chemical. This is a stable low-pH safe acid with less risk of off-gassing than the commonly used hydrochloric acid blends used in OLR's, chillers, and finishing chillers.

III. Residual Studies

Study I: Evaluation of potential chemical residuals

A study was conducted in which two groups of ready-to-cook chicken carcasses (5 each for a total of 10 carcasses) were collected from a commercial processing plant. The 5 control carcasses were sprayed with tap water and the 5 treated carcasses were sprayed with AFTEC 3000 at a pH of 2.0 (use dilution strength) for 5 seconds and allowed to drip for 2 minutes (to simulate actual poultry processing line conditions prior to the carcasses entering the chill system). Then the 5 control carcasses and the 5 treated carcasses were placed into separate containers with 30 gallons of ice water that was agitated using compressed air for 1 hour, to simulate commercial poultry chilling.

After chilling, the skin, fat, and meat of each carcass was aseptically excised, placed into sterile plastic bags on ice, and transported to the University of Georgia Water and Soil Test Lab for evaluation of the components in AFTEC 3000 (sulfur from sulfuric acid and sodium from sodium sulfate) and compared to controls to determine if any chemical residuals were present in the skin, fat, or meat of the carcasses.

Sodium: Samples were prepared using EPA Method 3052 "Microwave assisted digestion of siliceous and organically based matrices" and then evaluated using EPA Method 6010B "Inductively-coupled plasma atomic emission spectrometry."

Sulfuric acid: Samples were prepared using EPA Method 3052 "Microwave assisted digestion of siliceous and organically based matrices" and then evaluated using EPA Method 6010B "Inductively-coupled plasma atomic emission spectrometry."

The raw data results in parts per million (ppm) of the residual studies are presented in Table 1 below.

AFT 3000 Residual Data

Item	Compound	Number	Control	Treated	P Value
Skin	Sulfur	1	12.4	7.58	
Skin	Sulfur	2	4.3	8.29	
Skin	Sulfur	3	6.42	11.2	
Skin	Sulfur	4	11.3	14.2	
Skin	Sulfur	5	6.95	10.4	
			8.274	10.334	0.3173
Fat	Sulfur	1	6.41	11.1	
Fat	Sulfur	2	11.8	12.5	
Fat	Sulfur	3	10.5	11	
Fat	Sulfur	4	9.57	14.2	
Fat	Sulfur	5	9.27	11	
			9.51	11.96	0.0549
Meat	Sulfur	1	24.9	28.9	
Meat	Sulfur	2	30.7	20.6	
Meat	Sulfur	3	16.3	24.8	
Meat	Sulfur	4	19.3	26.7	
Meat	Sulfur	5	29.9	21.8	
			24.22	24.56	0.9187

Item	Compound	Number	Control	Treated	
Skin	Sodium	1	155	207	
Skin	Sodium	2	98.6	94.3	
Skin	Sodium	3	82.4	202	
Skin	Sodium	4	115	207	
Skin	Sodium	5	102	137	
			110.6	169.46	0.0538
Fat	Sodium	1	112.4	112.1	
Fat	Sodium	2	109	123.4	
Fat	Sodium	3	80.1	115	
Fat	Sodium	4	88.9	91.1	
Fat	Sodium	5	84.7	121.8	
			95.02	112.68	0.0785
Meat	Sodium	1	306	242	
Meat	Sodium	2	378	254	
Meat	Sodium	3	360	397	
Meat	Sodium	4	341	361	
Meat	Sodium	5	303	260	
			337.6	302.8	0.3493

The means for each part (skin, fat, or meat) were compared (control vs. treated) for each chemical component (sulfur or sodium) using ANOVA. These data demonstrate that no significant differences ($P \leq 0.05$) were observed between post-chill chicken skin, fat, or meat samples that were treated with tap water (controls) or treated using AFTEC 3000 in a spray solution prior to chilling. Thus, it may be concluded that no chemical residual exists on the skin, fat, or meat of chicken carcasses treated using AFTEC 3000 in a spray solution prior to chilling.

Because of these results, Advanced Food Technologies, LLC (AFT) feels that use of AFTEC 3000 as an antimicrobial at various locations throughout processing would not pose any risk of leaving any chemical residual on chicken skin, fat, or meat.

Study II: Evaluation of the ability of AFTEC 3000 to have a residual impact on aerobic plate counts or psychrotrophic plate counts (spoilage bacteria) after treatment and storage of poultry.

A study was conducted to determine if treating carcasses with AFTEC 3000 had any residual impact on bacteria during storage.

The procedure used was as follows:

Eighty carcasses were collected before the online reprocessing system in a commercial poultry operation. These carcasses were transported to the Poultry Research Center at the University of Georgia. The carcasses were separated into groups of 10 each and subjected to the following:

1) 10 carcasses were tested prior to any treatment as controls

2) 10 carcasses were sprayed with tap water using a commercial sprayer and allowed to hang on the line for 1 minute, then placed for 1 hour in tap water with ice and aeration, then sampled as chill controls

3) 10 carcasses were sprayed with tap water using a commercial sprayer and allowed to hang on the line for 1 minute, then sampled as spray controls

4) 10 carcasses were sprayed with tap water using a commercial sprayer and allowed to hang on the line for 1 minute, then placed for 1 hour in tap water with ice and aeration, then held for 24 hours at 4°C, and sampled as chill 24 h controls

5) 10 carcasses were sprayed with tap water using a commercial sprayer and allowed to hang on the line for 1 minute, then placed for 1 hour in tap water with ice and aeration, then held for 48 hours at 4°C, and sampled as chill 48 h controls

6) 10 carcasses were sprayed with AFTEC 3000 at a pH of 1.5 and allowed to sit for no longer than 1 minute, then sampled

7) 10 carcasses were sprayed with AFTEC 3000 at a pH of 1.5 and allowed to sit for no longer than 1 minute, then placed for 1 hour in tap water with ice and aeration, then held for 24 hours at 4°C, and sampled (AFTEC Chill 24 hr)

8) 10 carcasses were sprayed with AFTEC 3000 at a pH of 1.5 and allowed to sit for no longer than 1 minute, then placed for 1 hour in tap water with ice and aeration, then held for 48 hours at 4°C, and sampled (AFTEC Chill 48 hr)

9) Carcasses were sampled using 400 mL of 0.1% buffered peptone water with neutralizer

10) Rinses were diluted and plated onto 2 sets of Petrifilm Aerobic Count Plates

11) 1 set of plates was incubated at 37°C for 48 hours and counted (APC Counts)

12) 1 set of plates was incubated at 7°C for 10 days and counted (psychrotrophic plate counts)

13) Means for each group were graphed and compared using the ANOVA procedure of SAS

Results:

The results obtained in this study are presented in Figures 1 and 2 below:

Figure 1

The effect of spraying tap water or AFTEC 3000 on broiler carcasses and testing immediately, or after storage for 24 or 48 hours on aerobic plate counts (APC)

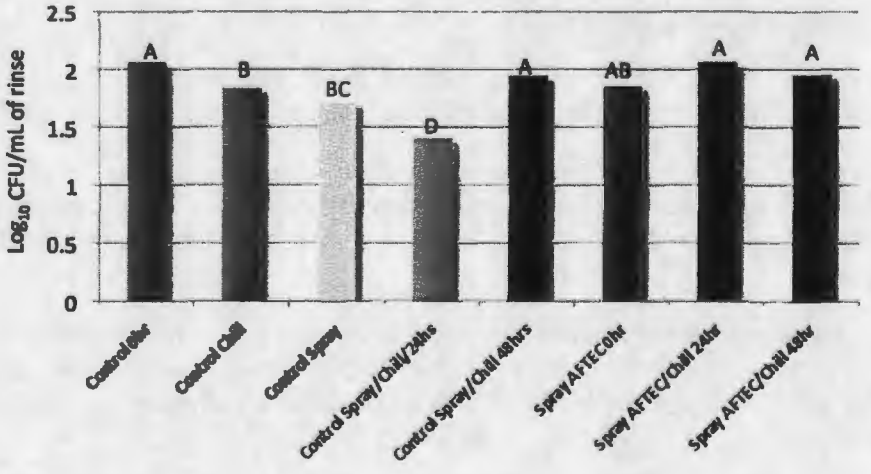
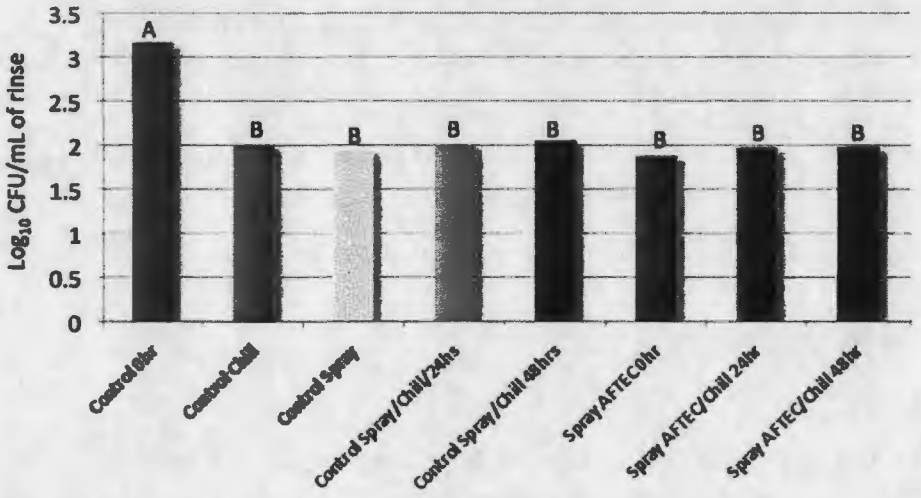


Figure 2

The effect of spraying tap water or AFTEC 3000 on broiler carcasses and testing immediately, or after storage for 24 or 48 hours on psychrotrophic plate counts (PPC)



These data indicate that even though AFTEC 3000 was sprayed onto carcasses, no additional reductions in aerobic plate counts (APC) or psychrotrohic plate counts (Spoilage bacteria-PPC) were observed for carcasses when compared any other group except the original control (untreated group). Moreover, and most importantly, APC and PPC bacteria on carcasses sprayed with AFTEC 3000 and tested immediately, after 24 hours of storage, or after 48 hours of storage were not significantly different. This means that no residual effect on spoilage bacteria would occur if carcasses treated with AFTEC 3000 were stored.

IV. Antimicrobial Studies

Numerous studies have been conducted at several different poultry processing plants at different times during the past year:

- Study 1 is an in-plant post chill spray system comparing 40 treated and 40 control carcasses.
- Study 2 is an in-plant commercial finishing chiller comparing 10 treated and 10 control carcasses.
- Study 3 was another post-chill spray cabinet test using 10 control and 10 treated carcasses.

- Study 4 was a lab study simulating a post-chill dip using inoculated *Salmonella* carcasses. A total of 30 carcasses were used in this study.
- Study 5 was an in-plant study of a commercial installation of AFTEC 3000 as an intervention placed between the OLR and the chiller in a poultry plant that was struggling in a USDA set. The intervention was a spray/dip combination.
- Study 6 was the same Study 5 plant after the USDA set. A new post-chiller finishing chiller was installed with AFTEC as the anti-microbial dip. The post-OLR/pre-chill dip tank was shortened and the spray cabinets removed.
- Study 7 was an in-plant comparison of AFTEC 3000 in spray cabinets at the New York Rinse (NYR) and pre-OLR.

Studies 1-3 are analyzed and summarized as a group (early studies). Studies 4-7 are each analyzed and discussed separately.

Study 1: Evaluation of AFTEC 3000

Approach:

1) In Plant 1, ten carcasses within a given flock, were removed from the line just after chilling using sterile gloves, sprayed with tap water using a hand-held sprayer, and these carcasses were termed Post-Chill Controls (PCC). Ten carcasses were allowed to traverse through a post-chill spray system, and collected from the line using sterile gloves. These carcasses were termed Post-chill AFTEC 3000 spray (PTC).

2) After allowing the carcasses to drip thoroughly, all carcasses were individually bagged in sterile polyethylene bags and rinsed using 400 ml of sterile Butterfield's phosphate buffer containing neutralizing buffer (Neutralizing Buffer - Formula per one liter of distilled water 0.0425g KH_2PO_4, 0.16g $Na_2S_2O_3$, 5.0g aryl sulfonate complex pH adjusted to 7.2 ± 0.2 at 25°C). This rinsate neutralized any residual AFTEC 3000 that may be rinsed from the carcass. The rinsates were encoded using a 4 digit number (to prevent identification by Silliker Laboratory employees and the introduction of bias) and sent on blue ice in a cooler using FedEx to Silliker Laboratories for evaluation for APC, *E. coli* counts, and *Salmonella* prevalence.

3) This procedure was conducted 4 times on 4 separate days such that 40 carcasses were collected before and after post-chill spraying for a total of 80 carcasses.

4) The post-chill spray consisted of tap water dosed with AFTEC 3000 to a target pH level of 1.5 ± 0.2.

5) Microbiological tests conducted included aerobic plate counts (APC), *Escherichia coli* (*E. coli*) counts, and *Salmonella* prevalence tests (% positive).

6) Encoded microbiological results were received from Silliker labs and submitted to the Department of Statistics at The University of Georgia for analysis.

Study 2: Evaluation of AFTEC 3000

Approach:

1) In Plant 2, ten carcasses within a given flock, were removed from the line just after chilling using sterile gloves, dipped into tap water, and these carcasses were termed Post-Chill Controls (PCC). Ten carcasses were allowed to traverse through a post-chill dip system for 30 seconds, and collected from the line using sterile gloves. These carcasses were termed Post-chill AFTEC 3000 Dip (PTD).

2) After allowing the carcasses to drip thoroughly, all carcasses were individually bagged in sterile polyethylene bags and rinsed using 400 ml of sterile Butterfield's phosphate buffer containing neutralizing buffer (Neutralizing Buffer - Formula per one liter of distilled water 0.0425g KH_2PO_4, 0.16g $Na_2S_2O_3$, 5.0g aryl sulfonate complex pH adjusted to 7.2 ± 0.2 at 25°C). This rinsate neutralized any residual AFTEC 3000 that may be rinsed from the carcass. The rinsates were encoded using a 4 digit number (to prevent identification by Silliker Laboratory employees and the introduction of bias) and sent on blue ice in a cooler using FedEx to Silliker Laboratories for evaluation for APC, *E. coli* counts, and *Salmonella* prevalence.

3) This procedure was conducted 1 time such that 10 carcasses were be collected before and after post-chill dipping for a total of 20 carcasses.

4) The post-chill spray consisted of tap water dosed with AFTEC 3000 to a target pH level of 1.5 ± 0.2.

5) Microbiological tests conducted were total aerobic plate counts (APC).

6) Encoded microbiological results were received from Silliker labs and submitted to the Department of Statistics at The University of Georgia for analysis.

Study 3: Evaluation of AFTEC 3000

Approach:

1) In Plant 3, ten carcasses within a given flock, were removed from the line just after chilling using sterile gloves, sprayed with tap water using a hand-held sprayer, and these carcasses were termed Post-Chill Controls (PCC). Ten carcasses were allowed to traverse through a post-chill spray system, and collected from the line using sterile gloves. These carcasses were termed Post-chill AFTEC 3000 spray (PTC).

2) After allowing the carcasses to drip thoroughly, all carcasses were individually bagged in sterile polyethylene bags and rinsed using 400 ml of sterile Butterfield's phosphate buffer containing neutralizing buffer (Neutralizing Buffer - Formula per one liter of distilled water 0.0425g KH_2PO_4, 0.16g $Na_2S_2O_3$, 5.0g aryl sulfonate

complex pH adjusted to 7.2 ± 0.2 at 25°C). This rinsate neutralized any residual AFTEC 3000 that may be rinsed from the carcass. The rinsates were encoded using a 4 digit number (to prevent identification by Silliker Laboratory employees and the introduction of bias) and sent on blue ice in a cooler using FedEx to Silliker Laboratories for evaluation for APC, *E. coli* counts, and *Salmonella* prevalence.

3) This procedure was conducted 1 time such that 10 carcasses were be collected before and after post-chill spraying for a total of 20 carcasses.

4) The post-chill spray consisted of tap water dosed with AFTEC 3000 to a target pH level of 1.5 ± 0.2.

5) Microbiological tests conducted included aerobic plate counts (APC), *Escherichia coli* (*E. coli*) counts, and *Salmonella* prevalence tests (% positive).

6) Encoded microbiological results were received from Silliker labs and submitted to the Department of Statistics at The University of Georgia for analysis.

Description of the experimental design, including the methods for control of bias:

All carcasses were selected from the line or after the post-chill dip using a pick one, count five and select the sixth carcass method to avoid bias. All carcass rinses were encoded using 4 digit number so that the laboratory technicians and statistician were not aware of which treatment corresponded to each sample.

Test method references:

Aerobic Plate Counts (APC) were determined using The Official Methods of Analysis of the AOAC, Method 990.12, and reported in colony forming units (CFU).
E. coli – *E. coli* were conducted using The Official Methods of Analysis of the AOAC, Method No. 998.08, and reported in colony forming units (CFU).
Salmonella – *Salmonella* were tested using The Official Methods of Analysis of the AOAC, Method No. 2000.07, and reported as either positive or negative.

Statistical methods:

Statistical evaluation was conducted by the Statistical Consulting Group in the Department of Statistics at the University of Georgia. Treatment effects were determined using t-tests and the Statistical Analytical Software (SAS) program for APC and *E. coli* counts. For *Salmonella* prevalence, logistical regression or Fisher's exact test was conducted using SAS.

Results and Discusson:

Results for Studies 1, 2, and 3 are presented in Tables 2, 3, and 4, respectively.

Table 2: Study 1 Effect of AFTEC 3000 used in a post-chill spray application on aerobic plate counts (APC), *E. coli* counts (*E. coli*), and *Salmonella* prevalence on broiler chicken carcasses in a commercial processing facility.

Treatment	Rep	APC	P value	*E. coli*	P value	*Salmonella* percent incidence	P value
Post-Chill Control	1	2.45		0.68		30	
Post-Chill Spray	1	1.05	0.0000006	0.03	0.0000007	0	<0.05
Post-Chill Control	2	2.39		0.56		0	
Post-Chill Spray	2	0.21	<0.000001	0.00	0.0038	0	NS
Post-Chill Control	3	2.20		0.58		10	
Post-Chill Spray	3	0.00	<0.000001	0.00	0.0051	0	<0.05
Post-Chill Control	4	1.23		0.03		0	
Post-Chill Spray	4	0.08	0.0005	0.00	0.3306	0	NS
Overall			<0.00001		0.0000007		<0.05
N		10		10		10	

Table 3: Study 2 Effect of AFTEC 3000 used in a post-chill dip application on aerobic plate counts (APC) on broiler chicken carcasses in a commercial processing facility.

Treatment	Rep	APC	P value
Post-Chill Control	1	1.89	
Post-Chill Dip	1	0.05	<0.0000001
N		10	

Table 4: Study 3 Effect of AFTEC 3000 used in a post-chill spray application on aerobic plate counts (APC), *E. coli* counts (*E. coli*), and *Salmonella* prevalence on broiler chicken carcasses in a commercial processing facility.

Treatment	Rep	APC	P value	*E. coli*	P value	*Salmonella*	P value
Post-Chill	1	2.11		0.74		20	
Post-Chill Spray	1	0.71	0.0004	0.03	0.0185	10	<0.05
N		10		10		10	

The results in Study 1 (Table 2) demonstrate that AFTEC 3000 was effective for significantly reducing APC, *E. coli*, and *Salmonella* prevalence in all 4 repetitions except for *E. coli* in Rep 4. This is because the levels of *E. coli* on Post-Chill control samples were extremely low at 0.03 $\log_{10}$ cfu/ml. With controls being this low, it is impossible to show a reduction in *E. coli*. The *Salmonella* prevalence in Reps 2 and 4 was also not reduced by AFTEC 3000 because there were no *Salmonella* detected on the controls in these Reps. The results for Study 2 (Table 3) indicate that APC was significantly reduced on poultry carcasses dipped in AFTEC 3000 for 20-30 seconds. Study 3 (Table 4) clearly demonstrated that AFTEC 3000 was effective for significantly reducing APC, *E. coli*, and *Salmonella* prevalence on chicken carcasses sprayed in a post-chill spray application on-line in a commercial processing plant. These data from Studies 1-3 demonstrate that AFTEC 3000 is an effective antimicrobial for use in poultry processing, whether used in a post-chill spray or dip application.

Study 4: Evaluation of AFTEC 3000 for reducing *Salmonella* on broiler chicken carcasses

A research study was conducted to determine the effect of Sulfuric Acid and Sodium Sulfate (AFTEC 3000) on *Salmonella* firmly attached to the surface of broiler chicken carcasses from a commercial processing facility.

Procedure:

1) Thirty eviscerated ready-to-cook chicken carcasses were collected just prior to the online reprocessing system in a large poultry processing facility.

2) The carcasses were transported to the Poultry Research Center at The University of Georgia for analysis.

3) To preclude counting native *Salmonella* that may already be attached to carcasses and vary considerably from carcass to carcass, each of the 30 carcasses were inverted and suspended from a shackle in the pilot poultry processing facility, inoculated with 0.1mL of an actively growing culture of nalidixic acid-resistant *Salmonella* Typhimurium (10^5 concentration) obtained from the USDA-Agricultural Research Service in Athens, GA.

4) After inoculation, the *Salmonella* were allowed to attach for a period of 1 hour to ensure that they were firmly attached.

5) Ten carcasses were tested immediately without dipping in water as untreated controls.

6) Ten carcasses were dipped in potable water for 25 seconds as a water control.

7) Ten carcasses were dipped in a solution of Sulfuric Acid and Sodium Sulfate (pH 1.54) for 25 seconds.

8) All carcasses were dipped and agitated during the treatment to imitate the agitation action in a post-chill dip system.

9) Each carcass was re-suspended on shackles for two minutes prior to bagging and rinsing with 400 mL Butterfield's Phosphate Buffer.

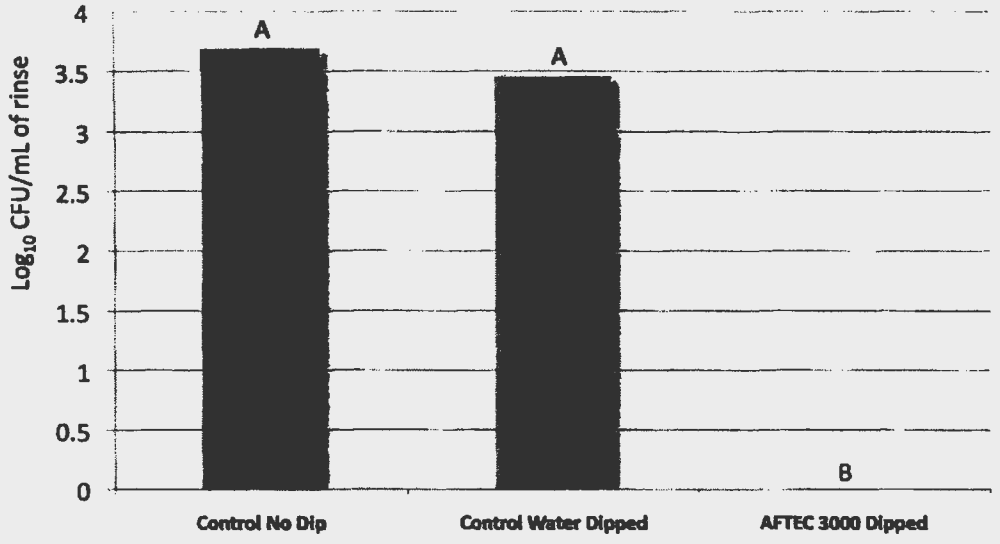
10) Samples were plated on BGS agar supplemented with nalidixic acid.

Results:

The data demonstrating the effect of Sulfuric Acid and Sodium Sulfate (AFTEC 3000) on *Salmonella* Typhimurium firmly attached to the surface of broiler chicken carcasses are presented in Figure 3:

Figure 3

The effect of dipping broiler carcasses in water or AFTEC 3000 on *Salmonella* Typhimurium counts



Study 5: Evaluation of AFTEC 3000 as a Pre-Chill dip followed by a Pre-Chill spray

A research study was conducted to determine if a sulfuric acid, sodium sulfate blended product (AFTEC 3000) was effective as an antimicrobial treatment when used prior to the chiller system at a pH of 2, when used as a pre-chill dip followed by a pre-chill flood. Total contact time of the treatment on the carcasses before entering the chiller was 45 seconds to one minute. This Facility was in a USDA "A" set with 38 samples of 51 total and 8 positive results. For the first 38 samples the facility was using an approved anti-microbial as its OLR, Pre-Chill dip, Pre-Chill spray and in the chiller. It was felt that something should be done to assure that 13 positive of the 51 were not reached. The plant replaced the previous anti-microbial in the Pre-Chill dip system and the subsequent Pre-chill cabinet that flooded carcasses with AFTEC 3000.

Experimental Design: Carcasses were sampled at three locations, Post-OLR but prior to the Pre-Chill dip, before the chiller after the Pre-Chill spray, and after the chiller, (Post-Chill). Carcasses were rinsed using the whole carcass rinse technique (400 mL buffered peptone water) as per USDA-FSIS protocol. Ten carcasses were sampled daily at each location for six days, (3 locations x 10 carcasses x 6 days = 180 total samples). Rinses were evaluated for APC counts and *Salmonella* spp. Presence

or absence. Samples were pulled simultaneously at the Post-OLR and Pre-Chill sites, however the post chill carcasses were taken after a 100 minute time lapse from the time the Pre-Chill sampling began so as to allow the sampling of the relatively same lot of carcasses that were sampled Pre-Chill.

Statistical Analyses: APC count data were $\log_{10}$ transformed prior to analyses so that the data would more closely meet the underlying assumptions of the Analysis of Variance, (ANOVA). Prior to transformation values of zero or <1 were changed to 0.1 since the $\log_{10}$ transformation of zero is undefined. APC count data was analyzed by an ANOVA with the aid of SAS, (Statistical software) and *Salmonella* spp. prevalence was analyzed using a 2 by 3 Chi Square test using the Tables option of the PROC FREQ procedure of SAS.

Results: APC levels were significantly highest before entering the Post-OLR dip and significantly the lowest exiting the chiller, (Table 5). For Salmonella spp. incidence, the carcasses prior to the Post-OLR dip were significantly higher than the other two sites. Four positive carcasses were found Pre-Chill after the dip and flood, and 2 positives were found after the chiller, (Table 6), there was not a large enough difference between the Pre-Chill and Post-Chill values to detect a significant difference.

Table 5. Average Aerobic Plate Counts at three locations in the plant.

Plant Location	Aerobic Plate Counts	Log_{10} Aerobic Plate Counts
Post-OLR (Base level)	5012	3.70[a]
Pre-Chill (AFTEC treated)	288	2.46[b]
Post-Chill	40	1.60[c]

Table 6. *Salmonella* prevalence at three locations in the plant.

	Locations		
Salmonella	Post-OLR (control)	Pre-Chill (treated)	Post-Chill
Number Positive	15	4	2
Number Negative	45	56	58
Percent Positive	25%	7%	3%

Discussion: The AFTEC Post-OLR dip followed by an AFTEC Pre-Chill spray was effective at reducing microbiological counts and *Salmonella* spp. frequency. Since its placement on the evisceration lines at this facility, zero carcasses sampled by the

USDA were found to be positive for *Salmonella* spp. Another observation was that no product defects occurred.

Study 6: Effect of AFTEC 3000 on Aerobic Plate Counts and *Salmonella* spp. prevalence on chicken carcasses treated during Pre-Chill, Chilling, and in the Finishing Chiller.

A study was conducted to evaluate the effect of AFTEC 3000 on Aerobic Plate Counts at 5 locations and *Salmonella* spp. percentages at 2 locations after evisceration in a poultry processing facility where the Pre-Chill Dip, the Chiller and the Finishing Chiller were acidified.

This Study VI was conducted in the same plant as Study V after the USDA-FSIS had taken their sample set for *Salmonella*. A new post-chiller finishing chiller (Morris) was installed with AFTEC as the anti-microbial dip. The post-OLR/pre-chill dip tank was shortened and the spray cabinets removed. A commercial chiller management system (Hope Technical) was installed to manage chlorine dosage and the use of AFTEC acid to targeted pH and ORP settings.

Experimental Design: Carcasses were sampled at five locations:1) Pre-OLR; 2) Post-OLR but prior to the AFTEC Pre-Chill dip; 3) after the AFTEC dip at pH 2.0 and before the chiller; 4) after the chiller, but before the finishing chiller (labelled Post-Chill); and 5) after the AFTEC treated finishing chiller (pH of 1.7-1.8) labelled as Post Finish. Carcasses were rinsed using the whole carcass rinse technique (400 mL buffered peptone water) as per USDA-FSIS protocol. Ten carcasses were sampled at each location for one production day, (5 locations x 10 carcasses x 1 day = 50 total samples). Rinses were evaluated for APC counts and *Salmonella* spp. presence or absence. Samples were pulled simultaneously at thePre-OLR, Post-OLR and Pre-Chill sites; however the Post-Chill and Post-Finish carcasses were taken after a 100 minute time lapse from the time the Pre-Chill sampling began so as to allow the sampling of the relatively same lot of carcasses that were sampled pre-chill.

Statistical Analysis: Count data were analyzed by analysis of variance, (ANOVA) using the proc GLM procedure of SAS statistical software. Prior to analyses counts were $\log_{10}$ transformed so that the data met the underlying assumption of the ANOVA. When differences among means were detected, means were separated using Duncan's multiple range test. Since a zero dilution was used for some locations, when zero colony forming units were found a value of 0.1 replaced >1 for purposes of analyses. Since only one sample was detected positive for *Salmonella* spp. at the Pre-OLR location, no statistical analysis was performed on *Salmonella* spp. results (Figure 4).

Results: Aerobic Plate Counts (APC) were steadily decreased along the process from Pre-OLR to Post-Finishing Chiller (Figure 5). The OLR itself did not show a significant decrease, but with a larger sample size the decrease seen across the OLR would have most likely been significant. Pre-Chill carcasses had significantly lower counts than Pre-OLR carcasses though not different from Pre-Dip counts, again

sample size was probably the reason. The final two locations, Chiller and Finishing Chiller reduced counts by a full log, (90% reductions), and these were significant reductions.

Figure 4. Percent *Salmonella spp.* Positive by Location

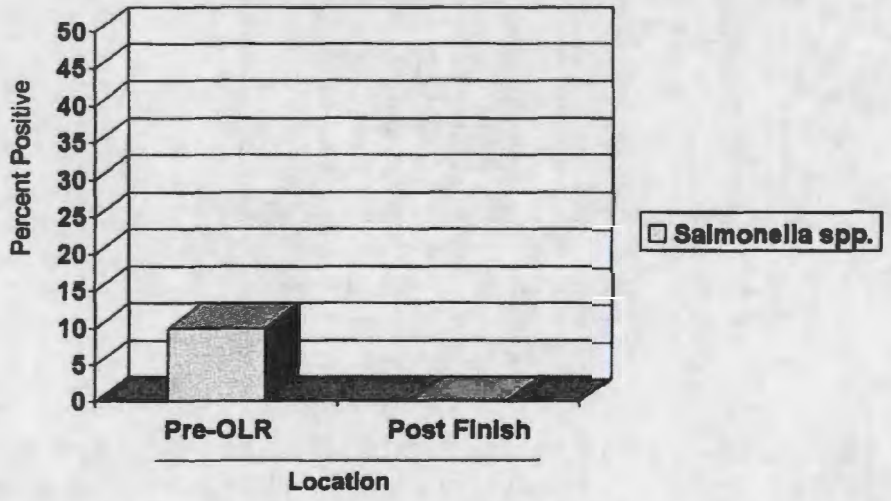
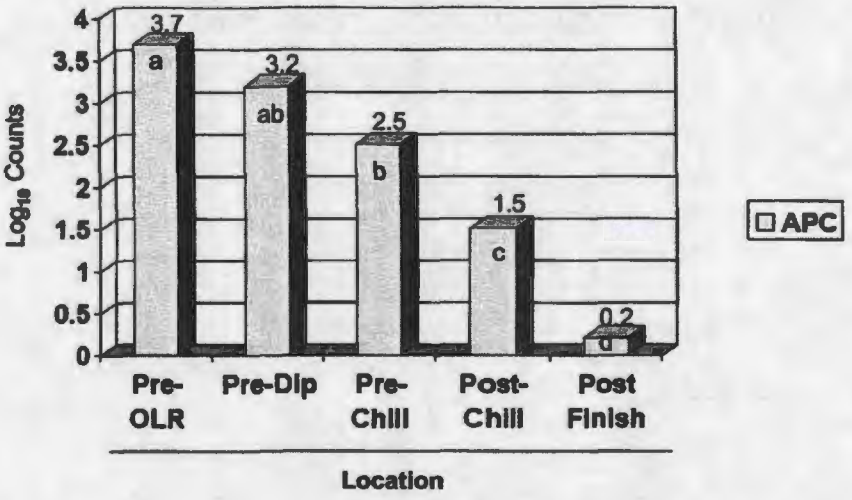


Figure 5. Mean Log_{10} Aerobic Plate Counts by Location



Study 7: An evaluation of the effect of AFTEC 3000 on Aerobic Plate Counts and generic *E. coli* on broiler carcasses in a large poultry processing facility when used in a New York Rinse cabinet and as a Pre-OLR cabinet.

A study was conducted to evaluate the impact of AFTEC 3000 on Aerobic Plate Counts and generic *E. coli* on chicken carcasses that were treated using an on-line cabinet at the New York Rinse and as a pre-OLR cabinet in a large poultry processing facility.

Approach:

1) In Plant 7, ten carcasses within a given flock were removed from the line just prior to the NY Rinse cabinet using sterile gloves and these carcasses were termed NYR Controls. Ten carcasses were allowed to traverse through the NYR cabinet and were sprayed with an AFTEC solution at a pH of 1.6 and collected from the line using sterile gloves. These carcasses were termed NYR Treated (AFTEC 3000 spray).

A second cabinet was installed just prior to the existing OLR cabinet. This was used to mimic AFTEC in a OLR cabinet due to the placement on the line while still permitting the carcasses to subsequently pass through the existing OLR system. Ten carcasses were removed from the line just prior to the pre-OLR cabinet using sterile gloves and these carcasses were termed Pre-OLR Controls. Ten carcasses were allowed to traverse through the Pre-OLR cabinet and were sprayed with an AFTEC solution at a pH of 1.6 and collected from the line using sterile gloves. These

carcasses were termed Pre-OLR Treated(AFTEC 3000 spray). All carcasses were selected by the count 5 pick 6th method to eliminate bias.

2) After allowing the carcasses to drip thoroughly, all carcasses were individually bagged in sterile polyethylene bags and rinsed using 400 ml of sterile Butterfield's phosphate buffer containing neutralizing buffer (Neutralizing Buffer - Formula per one liter of distilled water 0.0425g KH_2PO_4, 0.16g $Na_2S_2O_3$, 5.0g aryl sulfonate complex pH adjusted to 7.2 ± 0.2 at 25°C). This rinsate neutralized any residual AFTEC 3000 that may be rinsed from the carcass. The rinsates were encoded using a 4 digit number (to prevent identification by Silliker Laboratory employees and the introduction of bias) and sent on blue ice in a cooler using FedEx to Silliker Laboratories for evaluation for APC and *E. coli* counts.

3) This procedure was conducted 1 time such that 10 carcasses collected before and after NY Rinse spraying and before and after Pre-OLR spraying for a total of 40 carcasses.

4) The spray consisted of tap water dosed with AFTEC 3000 to a target pH level of 1.6 ± 0.2.

5) Microbiological tests conducted included aerobic plate counts (APC) and *Escherichia coli* (*E. coli*) counts.

6) Encoded microbiological results were received from Silliker labs and submitted to The University of Georgia for analysis. The results are summarized in Table 7.

Table 7. Average Aerobic Plate Counts and E. coli

	Aerobic Plate Counts (Log_{10})		*E. coli* (Log_{10})	
	Control	Treated	Control	Treated
NY Rinse	4.62	3.41	1.49	0.86
Pre-OLR (NYR off)	4.34	2.82	1.57	0.26

Results and Discussion: When carcasses were treated using AFTEC 3000 in spray cabinets in commercial poultry operations, APC's were reduced by over 1.0 log_{10}. *E. coli* were also reduced by a significant amount. These results would indicate that AFTEC could be a good candidate for an OLR study.

Overall Summary:

The collective data in this report demonstrate that AFTEC 3000 is an effective antimicrobial when used as a dip or spray in a variety of applications for reducing total Aerobic Plate Counts, *E. coli* counts and *Salmonella* spp. prevalence on broiler chickens. Moreover, the data also show that treatment of carcasses with AFTEC 3000 does not result in chemical residuals being present on the carcasses and there was no residual impact on Aerobic Plate Counts or Psychrotrophic Plate Counts during storage. Therefore, Advanced Food Technologies, LLC (AFT) respectfully requests that the USDA-FSIS grant them a letter of no objection to allow the use of sulfuric acid and sodium sulfate blend (AFTEC 3000) as an antimicrobial agent for poultry processing.

Appendix A:

Raw Data for Efficacy of AFTEC 3000 in 3 separate studies.

Study I: Efficacy of AFTEC 3000 as a post-chill spray antimicrobial on APC and *E. coli* counts, and *Salmonella* prevalence on chicken carcasses.

	Total Aerobic Count		E.coli Count		Salmonella
Sample ID	CFU/ml	LOG	CFU/ml	LOG	1 = +, 0 = -
Post-Chill Control (Butterfield's Phosphate Buffer)					
1101	310	2.49	6	0.78	0
1102	360	2.56	4	0.60	0
1103	450	2.65	45	1.65	0
1104	260	2.41	2	0.30	1
1105	440	2.64	4	0.60	0
1106	200	2.30	8	0.90	0
1107	310	2.49	3	0.48	0
1108	90	1.95	1	0.00	0
1109	290	2.46	31	1.49	1
1110	310	2.49	1	0.00	1
Average		2.45		0.68	30.00%
Post-Chill Control (Butterfield's Phosphate Buffer)					
1201	270	2.43	18	1.26	0
1202	430	2.63	3	0.48	0
1203	280	2.45	1	0.00	0
1204	430	2.63	5	0.70	0
1205	290	2.46	1	0.00	0
1206	170	2.23	1	0.00	0

1207	110	2.04	37	1.57	0
1208	310	2.49	2	0.30	0
1209	460	2.66	5	0.70	0
1210	70	1.85	4	0.60	0
Average		2.39		0.56	0.00%
Post-Chill Control (Butterfield's Phosphate Buffer)					
1211	110	2.04	9	0.95	0
1212	110	2.04	1	0.00	0
1213	49	1.69	21	1.32	1
1214	220	2.34	2	0.30	0
1215	170	2.23	4	0.60	0
1216	73	1.86	1	0.00	0
1217	3100	3.49	44	1.64	0
1218	98	1.99	5	0.70	0
1219	170	2.23	1	0.00	0
1220	110	2.04	2	0.30	0
Average		2.20		0.58	10.00%
Post-Chill Control (Butterfield's Phosphate Buffer)					
1221	17	1.23	1	0.00	0
1222	4	0.60	1	0.00	0
1223	1	0.00	1	0.00	0
1224	1	0.00	1	0.00	0
1225	56	1.75	1	0.00	0
1226	250	2.40	2	0.30	0
1227	19	1.28	1	0.00	0
1228	170	2.23	1	0.00	0
1229	12	1.08	1	0.00	0
1230	49	1.69	1	0.00	0
Average		1.23		0.03	0.00%

Sample ID	Total Aerobic Count		E.coli Count		Salmonella
	CFU/ml	LOG	CFU/ml	LOG	1 = +, 0 = -
AFTEC 3804 Post-Chill Spray (Butterfield's Buffer) pH 1.51					
1121	21	1.32	1	0.00	0
1122	20	1.30	1	0.00	0
1123	26	1.41	2	0.30	0
1124	9	0.95	1	0.00	0
1125	3	0.48	1	0.00	0

1126	5	0.70	1	0.00	0
1127	2	0.30	1	0.00	0
1128	15	1.18	1	0.00	0
1129	5	0.70	1	0.00	0
1130	150	2.18	1	0.00	0
Average		1.05		0.03	0.00%
AFTEC 3000 Post-Chill Spray + Hand Spray(pH 1:39)					
1231	1	0.00	1	0.00	0
1232	1	0.00	1	0.00	0
1233	3	0.48	1	0.00	0
1234	1	0.00	1	0.00	0
1235	19	1.28	1	0.00	0
1236	1	0.00	1	0.00	0
1237	1	0.00	1	0.00	0
1238	1	0.00	1	0.00	0
1239	1	0.00	1	0.00	0
1240	2	0.30	1	0.00	0
Average		0.21		0.00	0.00%
AFTEC 3000 Post-Chill Spray + Hand Spray(pH 1:39)					
1241	1	0.00	1	0.00	0
1242	1	0.00	1	0.00	0
1243	1	0.00	1	0.00	0
1244	1	0.00	1	0.00	0
1245	1	0.00	1	0.00	0
1246	1	0.00	1	0.00	0
1247	1	0.00	1	0.00	0
1248	1	0.00	1	0.00	0
1249	1	0.00	1	0.00	0
1250	1	0.00	1	0.00	0
Average		0.00		0.00	0.00%
AFTEC 3000 Post-Chill Spray + Hand Spray(pH 1:39)					
1251	2	0.30	1	0.00	0
1252	1	0.00	1	0.00	0
1253	3	0.48	1	0.00	0
1254	1	0.00	1	0.00	0
1255	1	0.00	1	0.00	0

1256	1	0.00	1	0.00	0
1257	1	0.00	1	0.00	0
1258	1	0.00	1	0.00	0
1259	1	0.00	1	0.00	0
1260	1	0.00	1	0.00	0
Average		0.08		0.00	0.00%

Study II: Evaluation of AFTEC 3000 as an antimicrobial in a post-chill dip application, Plant 2.

	Total Aerobic Count	
	CFU/ml	LOG
Post-Chill Control		
1	820	2.91
2	26	1.41
3	55	1.74
4	74	1.87
5	99	2.00
6	53	1.72
7	270	2.43
8	35	1.54
9	49	1.69
10	38	1.58
Average	151.90	1.89

	Total Aerobic Count	
	CFU/ml	LOG
AFTEC 3000 Dip (30sec, pH 1.61-1.72, Buffered Peptone)		
1	37	1.57
2	21	1.32
3	40	1.60
4	8	0.90
5	37	1.57
6	12	1.08
7	22	1.34
8	18	1.26
9	14	1.15
10	5	0.70
Average	21.40	1.25

Study III: Evaluation of AFTEC 3000 as an antimicrobial in a post-chill spray cabinet, Plant 3.

	Total Aerobic Count		Total E.coli Count		Salmonella
	CFU/ml	LOG	CFU/ml	LOG	1 = +, 0 = -
Post-Chill Control					
1101	25	1.40	1	0.00	0
1102	260	2.41	12	1.08	0
1103	160	2.20	4	0.60	0
1104	32	1.51	1	0.00	1
1105	16	1.20	1	0.00	0
1106	340	2.53	2	0.30	0
1107	74	1.87	1	0.00	0
1108	6400	3.81	270	2.43	0
1109	180	2.26	62	1.79	0
1110	80	1.90	16	1.20	1
Average	756.70	2.11	37.00	0.74	20.00%
Post-Chill AFTEC 3000 Spray (pH 7.6)					
1111	6	0.78	1	0.00	0
1112	2	0.30	1	0.00	0
1113	6	0.78	2	0.30	0
1114	11	1.04	1	0.00	0
1115	7	0.85	1	0.00	1
1116	7	0.85	1	0.00	0
1117	11	1.04	1	0.00	0
1118	1	0.00	1	0.00	0
1119	4	0.60	1	0.00	0
1120	8	0.90	1	0.00	0
Average	6.30	0.71	1.10	0.03	10.00%

Study V: Sulfuric Acid/Sodium Sulfate blend as pre-chill dip/spray combination

Sample Description	APC		*Salmonella* sp.
	Count	log_{10}	
Pre-Dip Control	1910	3.3	Positive
Pre-Dip Control	2140	3.3	Positive
Pre-Dip Control	1650	3.2	Negative
Pre-Dip Control	700	2.8	Negative
Pre-Dip Control	590	2.8	Negative
Pre-Dip Control	2200	3.3	Positive
Pre-Dip Control	1790	3.3	Negative
Pre-Dip Control	4200	3.6	Positive
Pre-Dip Control	16700	4.2	Positive
Pre-Dip Control	2800	3.4	Negative
Pre-Dip Control	7600	3.9	Negative
Pre-Dip Control	8900	3.9	Negative
Pre-Dip Control	3800	3.6	Negative
Pre-Dip Control	4600	3.7	Negative
Pre-Dip Control	5000	3.7	Negative
Pre-Dip Control	20300	4.3	Negative
Pre-Dip Control	3300	3.5	Negative
Pre-Dip Control	6400	3.8	Negative
Pre-Dip Control	31000	4.5	Negative
Pre-Dip Control	49000	4.7	Negative
Pre-Dip Control	12600	4.1	Negative
Pre-Dip Control	11100	4.0	Negative
Pre-Dip Control	3300	3.5	Negative
Pre-Dip Control	9500	4.0	Negative
Pre-Dip Control	1860	3.3	Negative
Pre-Dip Control	3800	3.6	Negative
Pre-Dip Control	4500	3.7	Negative
Pre-Dip Control	5100	3.7	Positive
Pre-Dip Control	3700	3.6	Positive
Pre-Dip Control	2600	3.4	Positive
Pre-Dip Control	114000	5.1	Negative
Pre-Dip Control	7100	3.9	Negative
Pre-Dip Control	2500	3.4	Negative
Pre-Dip Control	6800	3.8	Negative
Pre-Dip Control	2310	3.4	Positive
Pre-Dip Control	2270	3.4	Negative
Pre-Dip Control	3300	3.5	Positive
Pre-Dip Control	34000	4.5	Negative
Pre-Dip Control	1080	3.0	Negative
Pre-Dip Control	265000 Est.	5.4	Negative
Pre-Dip Control	2350	3.4	Positive
Pre-Dip Control	20200	4.3	Negative
Pre-Dip Control	10800	4.0	Negative
Pre-Dip Control	2900	3.5	Negative
Pre-Dip Control	3500	3.5	Negative

Pre-Dip Control	2900	3.5	Negative
Pre-Dip Control	41000	4.6	Positive
Pre-Dip Control	12700	4.1	Positive
Pre-Dip Control	1790	3.3	Positive
Pre-Dip Control	2100	3.3	Negative
Pre-Dip Control	3900	3.6	Negative
Pre-Dip Control	990	3.0	Negative
Pre-Dip Control	4900	3.7	Negative
Pre-Dip Control	2700	3.4	Negative
Pre-Dip Control	5000	3.7	Negative
Pre-Dip Control	4200	3.6	Negative
Pre-Dip Control	4100	3.6	Positive
Pre-Dip Control	1510	3.2	Negative
Pre-Dip Control	6500	3.8	Negative
Pre-Dip Control	10000	4.0	Negative
	AVG. =	**3.7**	**15/60 = 25.0%**

Post-Dip Treated	175	2.2	Negative
Post-Dip Treated	71	1.9	Negative
Post-Dip Treated	217	2.3	Negative
Post-Dip Treated	97	2.0	Negative
Post-Dip Treated	75	1.9	Negative
Post-Dip Treated	1210	3.1	Negative
Post-Dip Treated	35	1.5	Negative
Post-Dip Treated	78	1.9	Negative
Post-Dip Treated	67	1.8	Negative
Post-Dip Treated	178	2.3	Negative
Post-Dip Treated	480	2.7	Negative
Post-Dip Treated	4	0.6	Negative
Post-Dip Treated	182	2.3	Negative
Post-Dip Treated	180	2.3	Negative
Post-Dip Treated	1450	3.2	Negative
Post-Dip Treated	1770	3.2	Negative
Post-Dip Treated	10800	4.0	Negative
Post-Dip Treated	520	2.7	Negative
Post-Dip Treated	960	3.0	Negative
Post-Dip Treated	540	2.7	Negative
Post-Dip Treated	250	2.4	Negative
Post-Dip Treated	122	2.1	Negative
Post-Dip Treated	330	2.5	Negative
Post-Dip Treated	3300	3.5	Negative
Post-Dip Treated	164	2.2	Negative
Post-Dip Treated	1060	3.0	Negative
Post-Dip Treated	270	2.4	Negative
Post-Dip Treated	39000 Est.	4.6	Negative
Post-Dip Treated	370	2.6	Negative
Post-Dip Treated	500	2.7	Negative
Post-Dip Treated	260	2.4	Negative
Post-Dip Treated	171	2.2	Negative

Post-Dip Treated	55	1.7	Positive
Post-Dip Treated	95	2.0	Positive
Post-Dip Treated	118	2.1	Negative
Post-Dip Treated	136000	5.1	Negative
Post-Dip Treated	225	2.4	Negative
Post-Dip Treated	105	2.0	Negative
Post-Dip Treated	310	2.5	Positive
Post-Dip Treated	111	2.0	Negative
Post-Dip Treated	2200	3.3	Negative
Post-Dip Treated	750	2.9	Negative
Post-Dip Treated	220	2.3	Negative
Post-Dip Treated	800	2.9	Negative
Post-Dip Treated	98	2.0	Negative
Post-Dip Treated	400	2.6	Negative
Post-Dip Treated	540	2.7	Negative
Post-Dip Treated	480	2.7	Positive
Post-Dip Treated	260	2.4	Negative
Post-Dip Treated	140	2.1	Negative
Post-Dip Treated	1250	3.1	Negative
Post-Dip Treated	69	1.8	Negative
Post-Dip Treated	71	1.9	Negative
Post-Dip Treated	340	2.5	Negative
Post-Dip Treated	81	1.9	Negative
Post-Dip Treated	780	2.9	Negative
Post-Dip Treated	43	1.6	Negative
Post-Dip Treated	33	1.5	Negative
Post-Dip Treated	63	1.8	Negative
Post-Dip Treated	195	2.3	Negative
	AVG. =	**2.5**	**4/60 = 6.7%**

Post-Chill	67	1.8	Negative
Post-Chill	28	1.4	Negative
Post-Chill	19	1.3	Negative
Post-Chill	34	1.5	Negative
Post-Chill	9	1.0	Negative
Post-Chill	17	1.2	Positive
Post-Chill	12	1.1	Negative
Post-Chill	65	1.8	Negative
Post-Chill	16	1.2	Negative
Post-Chill	7	0.8	Negative
Post-Chill	9	1.0	Negative
Post-Chill	13	1.1	Negative
Post-Chill	7	0.8	Negative
Post-Chill	12	1.1	Negative
Post-Chill	3	0.5	Negative
Post-Chill	1490	3.2	Negative
Post-Chill	90	2.0	Negative
Post-Chill	27	1.4	Negative
Post-Chill	310	2.5	Negative

Post-Chill	13	1.1	Positive
Post-Chill	2	0.3	Negative
Post-Chill	1	0.0	Negative
Post-Chill	7	0.8	Negative
Post-Chill	15	1.2	Negative
Post-Chill	87	1.9	Negative
Post-Chill	106	2.0	Negative
Post-Chill	<1	0.0	Negative
Post-Chill	34	1.5	Negative
Post-Chill	123	2.1	Negative
Post-Chill	95	2.0	Negative
Post-Chill	28	1.4	Negative
Post-Chill	460	2.7	Negative
Post-Chill	45	1.7	Negative
Post-Chill	66	1.8	Negative
Post-Chill	210	2.3	Negative
Post-Chill	460	2.7	Negative
Post-Chill	81	1.9	Negative
Post-Chill	420	2.6	Negative
Post-Chill	49	1.7	Negative
Post-Chill	29	1.5	Negative
Post-Chill	250	2.4	Negative
Post-Chill	32	1.5	Negative
Post-Chill	79	1.9	Negative
Post-Chill	96	2.0	Negative
Post-Chill	38	1.6	Negative
Post-Chill	26	1.4	Negative
Post-Chill	37	1.6	Negative
Post-Chill	950	3.0	Negative
Post-Chill	46	1.7	Negative
Post-Chill	75	1.9	Negative
Post-Chill	19	1.3	Negative
Post-Chill	182	2.3	Negative
Post-Chill	290	2.5	Negative
Post-Chill	47	1.7	Negative
Post-Chill	4	0.6	Negative
Post-Chill	290	2.5	Negative
Post-Chill	33	1.5	Negative
Post-Chill	47	1.7	Negative
Post-Chill	530	2.7	Negative
Post-Chill	18	1.3	Negative
	AVG. =	**1.6**	**2/60 = 3.3%**

Study VII--cabinets

NEW YORK RINSE CABINET TEST

CONTROL SAMPLES

	Total Aerobic Count		E.coli	
	CFU/ml	LOG	CFU/ml	LOG
NYR Control (pulled post-NYR, cabinet OFF)				
1	120000	5.08	480	2.68
2	40000	4.60	610	2.79
3	160000	5.20	100	2.00
4	86000	4.93	40	1.60
5	10000	4.00	40	1.60
6	42000	4.62	0	0.00
7	22000	4.34	170	2.23
8	18000	4.26	100	2.00
9	30000	4.48	0	0.00
10	48000	4.68	0	0.00
Average	57600	4.62	154	1.49

TREATED SAMPLES

	Total Aerobic Count		E.coli	
	CFU/ml	LOG	CFU/ml	LOG
NYR Treated (pulled post-NYR cabinet ON at pH 1.5-1.6)				
1	560	2.75	30	1.48
2	290	2.46	0	0.00
3	710	2.85	0	0.00
4	11300	4.05	40	1.60
5	10000	4.00	170	2.23
6	2500	3.40	0	0.00
7	6000	3.78	50	1.70
8	600	2.78	0	0.00
9	8000	3.90	0	0.00
10	14000	4.15	40	1.60
Average	5396	3.41	33	0.86

SIMULATED OLR CABINET TEST

pre-OLR Control (NYR OFF)				
1	63000	4.80	250	2.40
2	28000	4.45	10	1.00
3	8000	3.90	270	2.43
4	90000	4.95	190	2.28
5	9600	3.98	10	1.00
6	46000	4.66	20	1.30
7	5200	3.72	110	2.04
8	100000	5.00	0	0.00
9	4700	3.67	10	1.00
10	20000	4.30	190	2.28
Average	37450	4.34	106	1.57

post-OLR Treated (pH 1.5-1.6)				
1	1200	3.08	10	1.00
2	800	2.90	0	0.00
3	210	2.32	0	0.00
4	1500	3.18	40	1.60
5	90	1.95	0	0.00
6	1200	3.08	0	0.00
7	370	2.57	0	0.00
8	900	2.95	0	0.00
9	1100	3.04	0	0.00
10	1200	3.08	0	0.00
Average	857	2.82	5	0.26

VI. Applicable prior approvals

United States Department of Agriculture | Food Safety and Inspection Service | Washington, D.C. 20250

Mr. Dennis Smithyman
President
Advanced Food Technologies, LLC
11230 Magnolia Glen
Shreveport, LA 71106

NOV 0 4 2008

Dear Mr. Smithyman:

This is in response to your October 30, 2008 email (Log number 08-NT-0387-N-A) requesting a letter from the Food Safety and Inspection Service (FSIS) stating that AFT Clear 3000 is the same as sodium bisulfate and under FSIS Directive 7120.1, "Safe and Suitable Ingredients Used in the Production of Meat and Poultry Products" can be used as an acidifier in meat and poultry plants.

After reviewing your submitted information, FSIS has determined that AFT Clear 3000 is considered the same as sodium acid sulfate (SAS) or sodium bisulfate and, thus, would not be considered new technology. SAS or sodium bisulfate is already permitted by FSIS to be used as a pH control agent (acidifier) in water used in meat and poultry processing sufficient for the purpose.

This letter should not be considered as validation that your process will be effective in any particular FSIS establishment. Your technology, as described in your notification, will need to be factored into an establishment's hazard analysis and, if appropriate, incorporated into its HACCP Plan or SSOP, or other prerequisite program, validated for its application, and verified on an ongoing basis for its effectiveness. If the establishment does not address the effects of using your technology in its hazard analysis, FSIS would be unable to determine that the product processed using your technology is safe, including microbiologically, not adulterated; and therefore, the product would not be eligible to bear the mark of inspection.

If you have any questions, please contact Dr. David Zeitz at (202)690-3556 or david.zeitz@fsis.usda.gov.

Sincerely,

[redacted]

Dr. John Hicks, Director
Risk and Innovations Management Division
Office of Policy and Program Development

FSIS Form 2630-9 (6/96) EQUAL OPPORTUNITY IN EMPLOYMENT AND SERVICE

VII. References

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14. **Cousin, M. A., J. M. Jay, and P. C. Vasavada,** 1992. Psychrotrophic microorganisms. *in*: Compendium of Methods for the Microbiological Examination of Foods. C. Vanderzant and D. F. Splittstoesser, ed. American Public Health Association, Washington, D. C. pp. 156-157.

VIII. Responses to questions posed by Dr. David Zeitz, USDA/FSIS/OPPD/RIMD, regarding these background studies for use of AFTEC 3000 (Log#10-OLR-0514-N-A)

The questions posed by USDA-FSIS are emboldened and the responses to the questions are posted below.

1. Please explain the reason for the variation of the 7 study designs,

i.e., the selection of carcass numbers, the microorganism selections,

and number of days.

AFTEC 3000 has been approved for use as an acidifier since November, 2008. Numerous studies have been conducted by various groups to ascertain applicability and effectiveness of AFTEC 3000 from several poultry interventions. Some of these have been laboratory studies, some have been quick in-plant assessments, and some were full in-plant validation studies. Sometimes the studies and methodologies were conducted by UGA professor Dr. Scott Russell, and other times the testing was directed and paid for by the local plant with their in-house corporate laboratory services.

Cost effectiveness and statistical significance was also usually considered. Thus, a small sample size for post-chill application usually did not include salmonella testing. Incidence levels would be expected to be low and therefore not have statistical significance in a small sample size.

Study 1 was for a commercial post-chill spray at a plant in Delmarva. UGA directed the study and validated the results. Study 3 was a month later re-test to ensure performance was maintained, which the short study confirmed (same methodologies).

Study 2 was a short APC test for a finishing chiller in a plant in GA that was switching to AFTEC 3000 from one of the hydrochloric acid blends. As this plant already had low salmonella incidence post-finishing chiller, the subsequent salmonella inoculation study (Study 4) was conducted at UGA labs on their behalf.

Studies 5 and 6 were conducted by the corporate laboratory of a major processor at one of their plants in AR. AFTEC 3000 was initially introduced as a post-OLR/pre-chill dip (Study 5). A new finishing chiller was later installed using AFTEC 3000 and the finishing chiller overflow was filtered and then recycled back to the post-OLR/pre-chill dip. AFTEC 3000 was also then used as the chlorine acidifier for the chiller. Study 6 biomapped the net results.

Study 7 was a quick APC study for a plant considering the use of AFTEC 3000 in the NYR cabinets and OLR cabinets (once AFTEC 3000 is approved for OLR application).

2. When tap water was used, do you know what antimicrobials were in the tap water and at what levels?

No specifics tests were conducted. All the plants were in districts where the city water is chlorinated. No tests were conducted in plants where the local water district uses mainly ammonia or chloramines. However, no difficulties would be expected from a chemical interaction standpoint.

3. This mirrors question 1 above. In Study 2 why were only 20 total carcasses selected and why was only APC's tested?

As mentioned above, Study 2 was a short APC test for a finishing chiller in a plant in GA that was switching to AFTEC 3000 from one of the hydrochloric acid blends (FreshFx). The plant only requested an APC test to prove reductions across the finishing chiller. As this plant already had low salmonella incidence post-finishing chiller, the subsequent salmonella inoculation study (Study 4) was conducted at UGA labs on their behalf.

4. Were controls and AFTEC testing done with both the NYR cabinet and pre-OLR cabinet running at the same time? If both were used at the same time during testing, it appears that the APC's and E. coli counts went up after the NYR cabinet and before the pre-OLR cabinet (Table 7).

No. Both cabinets were OFF for the Control samples. Thus, there was a greater than 1 log reduction in APC's across the treated (ON) NYR cabinet. With the NYR cabinet OFF, the pre-OLR controls were log 4.34 and after the OLR cabinet they were log 2.82. Thus, both AFTEC cabinets reduced APC's by over 1 log. A test was not conducted with both cabinets ON. We're sorry for the confusion in the write-up.

Attachment 5

Analysis of On-Line Reprocessing Results with Aftec 3000™ as an Antimicrobial Agent

Purpose: An on-line reprocessing (OLR) trial was conducted under a USDA waiver, (log # 10-OLR-0514-N-A) to determine if Aftec 3000™ is an effective antimicrobial agent in an OLR application. Aftec consists of sulfuric acid blended with sodium sulfate. The sulfate is a natural buffering salt that makes the acid solution easy to handle and prevents organoleptic damage to meats. Over a 10 day period, 400 carcasses were identified as being either visually uncontaminated (VC) or visually contaminated (VF). One hundred carcasses, ten per day per condition, were rinsed before and after the OLR.

Statistical Analysis: Aerobic plate count APC and *E. coli* colony forming units data were $\log_{10}$ transformed prior to analysis. Prior to transforming the numbers, values of zero or none detected were converted to the detection limit for that sample. For all cases, a 1:10 dilution was the lowest dilution level used, so a 10 replaced all zero or none detected observations. Count data were analyzed using an analysis of variance (ANOVA) with the aid of SAS (Cary, N.C.).

The statistical model used was:

$$Y_{ijkl}=\mu + D_i + C_j + L_k + C^*L_{(jk)} + \varepsilon_{ijkl}$$

Where: Y_{ijkl} is the result of the overall mean μ, plus the effect of the i^{th} Day[1], (I = 1, 2,..10), plus the effect of the j^{th} Carcass condition (Visually uncontaminated (VC) or visually contaminated (VF)), plus the effect of the k^{th} location (pre-OLR or post-OLR), plus the effect of the jk^{th} carcass condition by location interaction (pre-OLR, VC; pre-OLR, VF; post-OLR, VC: and post-OLR, VF), plus the effect of the $ijkl^{th}$ whole bird carcass rinse.

For *Salmonella spp.* only six positive samples were identified, four pre-OLR and two post-OLR. No differences would be detectable from such low incidence so no statistical tests were conducted. For this reason, only a descriptive analysis is presented for *Salmonella spp.*

Results: Carcass condition at a location did not have a significant impact on colony forming unit levels of APC or *E. coli* (Table 1). However, across the OLR system there were significant reductions in both APC and *E. coli*; both microbial class means pre-OLR were higher than post-OLR means (Figure 1).

For *Salmonella spp.*, few positive carcasses were detected; however, from a descriptive standpoint the trend was favorable. Four positive carcasses were detected pre-OLR and two positive carcasses were detected post-OLR, which demonstrates a 50 percent reduction in incidence. For both the VC and the VF carcasses the number of positive carcasses post-OLR was reduced by one from pre-OLR carcasses (Figure 2).

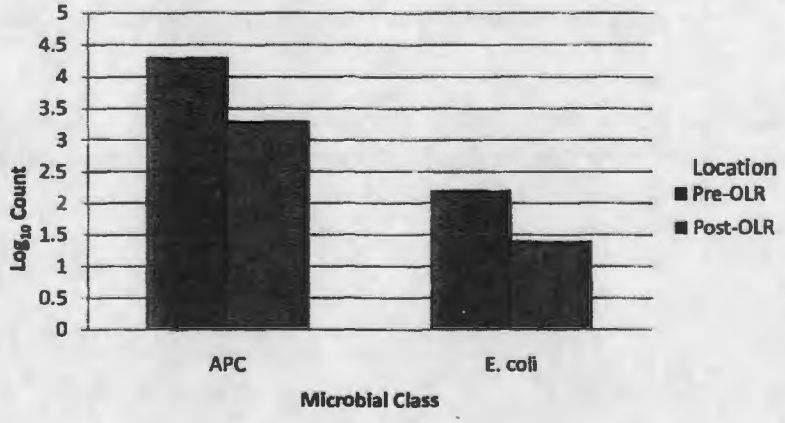
1. The original protocol stated data would be collected over a 9 day period, however, during the time from when the protocol was submitted to the time the data collection began, facilities were trying to get approved for Russian export. If the facility had to switch to an approved PAA the protocol was a ten day data collection period. The ten day collection period was mistakenly used for this protocol as well. The additional data collection enhances the trial.

Table 1. Mean log_{10} APC and *E. coli* counts by location and carcass condition[1]

	Microbial Group and Carcass Condition			
	APC		*E. coli*	
Location	VC	VF	VC	VF
Pre-OLR	4.28	4.35	2.17	2.30
Post-OLR	3.33	3.30	1.42	1.39

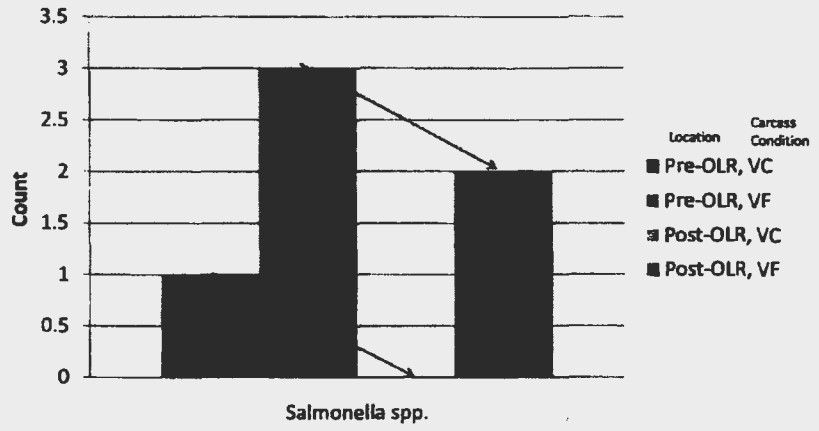
[1] For a microbial class at a location means were not significantly different ($p > 0.05$).

Figure 1. Mean log_{10} counts of APC and *E. coli* by location



[ab] Mean counts for a location within a microbial class were statistically different ($p \leq 0.05$).

Figure 2. Number of *Salmonella spp*. carcasses detected out of the 100 sampled per location and condition



Discussion: The APC and *E. coli* count numbers showed 90 and 85 percent statistically significant reductions from pre-OLR to post-OLR, respectively. *Salmonella spp.* showed a low positive incidence, so even though there was a 50 percent reduction in positive incidence post-OLR compared to pre-OLR, the reduction could not be shown to be significant. A similar trend was observed among all three microbial classes examined in this trial, which illustrates the importance of measuring pathogenic organisms and broader class indicator organisms.

Conclusion: The Aftec 3000™ product met the conditions for the waiver and is shown by these results to be an effective antimicrobial agent in the OLR. Additionally, since these data are satisfactory, the product should be granted waivers for two additional in-plant trials.

Attachment 6

USDA United States Department of Agriculture
Food Safety and Inspection Service

Office of Policy and Program Development

Risk and Innovations Management Division
George Washington Carver Center
5601 Sunnyside Ave: STOP 5271
Beltsville, MD 20705-5271

March 8, 2011

Dennis Smithyman
Advanced Food Technologies, LLC
11230 Magnolia Glen
Shreveport, LA 71106

Dear Mr. Smithyman:

This letter is in response to your February 7, 2011, revised notification requesting to conduct additional in-plant trials to "Evaluate the application of AFTEC 3000 (AFT Clear 3000) in commercial poultry on-line reprocessing for elimination of pathogenic and indicator populations of bateria. (Log No. 10-OLR-0514-N-B,C).

You have requested a waiver, pursuant under Title 9 of the Code of Federal Regulations 9 CFR §381.3 (b), to use AFTEC 3000 (AFT Clear 3000) On-Line Reprocessing (OLR) system on prechill poultry carcasses to conduct the second and third in-plant trials, pending Agency amendment of 9CFR §381.91(b) (1) [off-line reprocessing regulation].

In your notification, you requested permission to conduct simultaneously the second in-plant trial at Pilgrim's Pride, establishment # P6638, Enterprise, AL and the third in-plant trial at Gold'n Plump, establishment # P322, Cold Spring, MN following the revised February 3, 2011 protocol. You intend to conduct the study to test AFTEC 3000 (AFT Clear 3000) using a pH level of 1.8 (+/– 0.4).

FSIS has completed its review of your first in-plant trial data collected at Tyson Foods, Inc. establishment # P164, Forest, MS. The first in-plant trial data showed that the number of aerobic plate count (APC) bacteria, *Escherichia coli*, and *Salmonella* positive samples was statistically reduced after passage through the AFTEC 3000 (AFT Clear 3000) OLR system. The data showed that there was no statistical microbiological difference between carcasses marked visibly clean and those marked visibly contaminated after decontamination with the AFTEC 3000 (AFT Clear 3000) OLR treatment. Therefore, FSIS is granting you permission in lieu of 9CFR §381.91(b)(1) to conduct the second in-plant trial at establishment # P6638 and the third in-plant trial at establishment # P322, provided that:

1. Risk, Innovations, and Management Division (RIMD) receives data comparing microbiological levels of Aerobic Plate count (APC), *Escherichia coli* and *Salmonella* prevalence on two groups, marked visibly clean carcasses and

marked visibly contaminated carcasses **BEFORE** both have been treated with the AFTEC 3000 (AFT Clear 3000) OLR system.

2. RIMD receives data comparing microbiological levels of aerobic plate count (APC), *Escherichia coli* and *Salmonella* prevalence on two groups of marked visibly clean carcasses and marked visibly contaminated carcasses **AFTER** decontamination and both have been treated with the AFTEC 3000 (AFT Clear 3000) OLR system before they enter the chiller.

3. Data collected throughout the in-plant trial should be provided to the RIMD Project Manager (PM) for the Agency to examine using an Excel format. Final report on the results must be submitted in an Excel format to RIMD PM at the completion of the trial. The data must show results that are consistent with reduced microbiological and pathogen levels.

4. The parameters set forth in your revised February 3, 2011, OLR protocol, are followed. Operational parameters include:

   a. The dip tank or spray cabinet is fed continuously with tap water dosed with AFTEC 3000 (AFT Clear 3000) to a target pH level of 1.8 (+/- 0.4).

   b. For dip tanks, the fresh mixture will enter the tank at the bird exit end and counter flow through the tank to an overflow drain at the entrance end of the tank. The dip tank system will flow between 5 gal/minute and 10 gal/minute.

   c. For spray cabinets, the fresh mixture will be delivered to spray bars at a minimum pressure of 10 psi and flows between 5 gal/minute and 10 gal/minute.

5. The OLR system is validated in-plant to demonstrate that the establishment can apply it to obtain the anticipated effect under actual in-plant operational conditions as stated in the aforementioned protocol.

6. Establishment discusses the waiver and OLR system with the inspection program personnel (IPP), at the weekly meeting, prior to its implementation. The alternative procedures must be addressed in the Hazard Analysis and Critical Control Point (HACCP) plan, Sanitation Standard Operating Procedures (Sanitation SOPs), or a prerequisite program. In addition, establishments will need to explain how they intend to use the OLR system and where in the establishment's food safety system the procedures will be located.

   NOTE: The IPP will verify the procedures according to their location in the food safety system and verify whether the establishment is monitoring and documenting these parameters as described above. Once a week, IPP will use an appropriately scheduled PBIS procedure to verify one or more parts of the alternative procedures or parameters. IPP will verify whether the OLR

technology is operating in a manner that is consistent with this grant permission letter.

7. Establishment that does not have an existing OLR regulatory waiver under 9 CFR §381.3 (b) to use the OLR system must apply to the *Salmonella* Initiative Program (SIP), as detailed in Federal Register Notice 73FR4767, January 28, 2008, before a waiver for the use of the OLR system may be granted.

8. After the completion of the in-plant trials, establishment # P164, establishment # P6638, and establishment # P322 agrees to submission of ongoing microbiological monitoring results to RIMD at each quarter. RIMD will review the monitoring data to assess the ongoing effectiveness of your OLR system. Data should be submitted in an Excel format to RIMD.OLRD@fsis.usda.gov.

FSIS IPP will have access to FSIS intranet at RIMD NT & NI Summaries postings on the web page that describes the alternative procedures (parameters) for this OLR technology.

Carcasses extensively affected with contamination or mutilation are condemned by FSIS inspectors (9CFR §381.91) and these carcasses will not be allowed to enter the OLR system. Sanitary dressing of carcasses on the line must be maintained in a manner to minimize contamination, including internally contaminated carcasses going through the OLR system.

Carcasses that are normally subject to off-line reprocessing (OLR) can be reprocessed on-line and are subject to compliance with 9CFR §381.65 (e) and 9CFR §381.76 for Finished Product Standards (FPS). IPP will continue to conduct zero fecal tolerance and FPS checks.

This letter should not be considered as validation that your chemical or process would be effective in any particular official establishment.

Be aware that if establishment # P164, establishment # P6638, and establishment # P322 produces product that conflicts with the provisions of the Poultry Products Inspection Act (21 U.S.C. 451, et seq.) or has repeated Noncompliance Records (NRs) documenting failure to maintain the alternative procedures associated with this waiver, the waiver could be revoked.

Continuation of the in-plant trials will be granted based on evidence of a timely start, adherence to the schedule in the protocol, and appropriate progress towards the purpose stated in your protocol. If the in-plant trials do not commence within 90 calendar days of receipt of this letter, then the "Permission" status to start the in-plant trials will be withdrawn. You will need to submit in writing for an extension of time to commence the in-plant trials.

If you have any questions, please contact the PM, Dr. David Zeitz, at (321) 327-2576 or by e-mail at David.Zeitz@fsis.usda.gov. If you have any questions on SIP, please contact Dr. Isabel Arrington at Isabel.Arrington@fsis.usda.gov.

Sincerely,

(b) (6) [redacted]

William K. Shaw, Jr., Ph.D.
Director
Risk, Innovations, and Management Division
Office of Policy and Program Development

Attachment 7

Study title: Integral Anti-microbial Solution Application Systems Using a Ross Blade Tenderizer—Phase 1 and 2 results

Conducted by: Peter M. Muriana, Ph.D., Professor, Food Microbiology, Dept. of Animal Science, Oklahoma State University

Study dates: Report completed on April 2, 2011

Objective: to demonstrate significant reductions of E. coli O157:H7 in non-intact meat by spraying anti-microbial solutions directly on the surface of the meat just prior to blade tenderization.

Methodology: Phase 1—evaluate 14 submitted anti-microbial solutions by spraying E. coli O157:H7 inoculated beef discs in the Ross machine spray system and measuring reductions versus controls. Phase 2—utilizing the best 7 performing anti-microbial solutions, spray inoculated whole muscle cuts just prior to blade tenderization. Core out the meat and slice to create meat discs at measurable depths from the surface. Check for E. coli incidence in each meat disc to measure performance vs. untreated controls.

Results and discussion: In Phase 1, there were 5 chemical blends that achieved a 1.0 Log cfu/cm2 reduction (90%) from inoculated controls when measured in less than 1 hour from treatment. AFTEC was one of the 5 best. A total of 7 treatment chemicals, including AFTEC, were selected for Phase 2 testing.

In Phase 2, each surface inoculated whole muscle cut was cored in 4 places and each core was sliced into 4 sections below the surface. This yields a total of 16 samples for each treatment plus 16 for the untreated controls. When analyzed for E. coli presence, the control cut had 15 of 16 samples positive for E. coli O157:H7. The 7 treated cuts had incidence levels from 1 (best) to 10 (worst). AFTEC performed in the middle group (with the other acids) with a total of 8.

Thus, the study did confirm that there is a real risk of contaminated meat carrying the E.coli into the interior of the meat with blade tenderization. However, spraying the meat with an anti-microbial solution just prior to tenderization can significantly reduce the contaimination risk to the general poupulation (AFTEC 3000 being one of these solutions). Continuing studies will look to optimize the systems and improve the quantification of risks and reductions.

Technical Report

Integral Antimicrobial Solution Application on the Ross Blade Tenderizer

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Phase 1 & Phase 2 Results

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Graduate Students: Jackie Eager (Meat Science)
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Dinesh Babu, PhD (Food Micro)

Industry Issue: A current concern with blade tenderized beef is the potential to carry surface contamination (i.e., *E. coli* O157:H7) into steak cuts that may be prepared rare for consumption, presenting a potential health risk to consumers. The USDA-FSIS distinguishes such tenderized beef as 'non-intact' beef and declares that there should be antimicrobial interventions in place to eliminate (or reduce) surface *E. coli* O157:H7 prior to blade tenderization. Most recently, an outbreak linked to a supplier of blade tenderized beef has raised concern for this issue even further within the industry and the regulatory agency.

Objective(s):

Phase 1: To use sufficiently high inoculation levels of *E. coli* O157:H7 that we can determine process effectiveness of various antimicrobial spray treatments on beef surfaces.

Phase 2: To use practical inoculum levels of *E. coli* O157:H7 on subprimal beef surfaces followed by spray treatment and blade tenderization to demonstrate that entry does not occur, or is minimized, after interventions are applied (complements Phase 1).

Major Equipment. A Ross Industries Inc. blade tenderizer, equipped with a multi-nozzle spray system (integral product tank and positive displacement pump) will be supplied for use in 228 FAPC. The advantage of using this system is that it is the same equipment that is currently being developed for the meat industry involved with blade tenderization and therefore there is no question as to whether data obtained in this study will reflect spray treatment of commercial systems (i.e., identical spray system, number of nozzles, same water pressure, operating speed, and dosing rate).

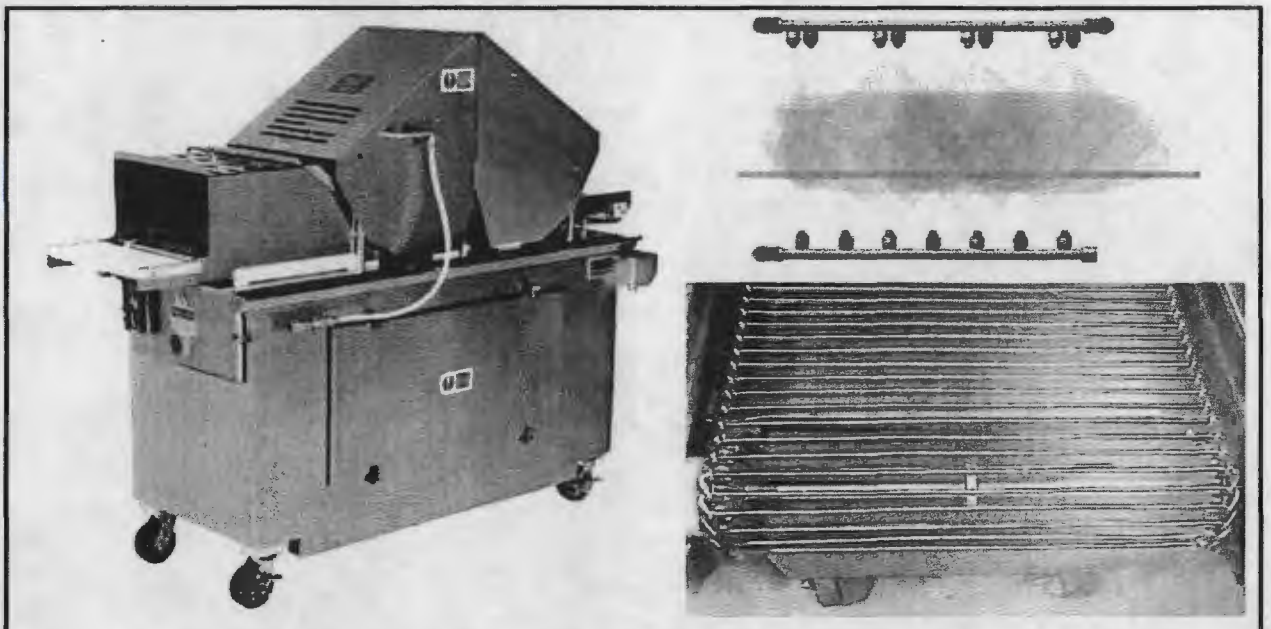


Figure 1. Photo and schematics of Ross tenderizer (TC700MC) with full coverage (top and bottom) spray system including the sani-grid conveyor belt.

Process Location 1 (228 FAPC). Initial processing was performed in 228 FAPC Bldg. Prior to the use of *E. coli* O157:H7 surface inoculants on beef products, protocols detailing experimentation and worker safety were submitted and approved by the Institutional Biosafety Committee (IBC) which designated 228 FAPC as a BSL-2 facility.

The use of inoculated beef samples (Phase 1: lean sirloin wafers; Phase 2: 10-15 lb sirloin top butts) and the potential for spray displacement of the inoculated organisms required the placement of the equipment in a secured and safe use location. Spray contact was minimized due to a shielded housing of the basic tenderizer machine. Personnel must wear designated PPE (personal protection equipment) when working with pathogens and sanitation regimens after each trial includes hot water spray, followed by hypochlorite spray and finally fogging of the entire room with a pressurized canister containing a quat sanitizer. BSL-2 status has been approved based on the safety precautions we implemented. This room is secured, is compatible with wall-to-floor spray sanitation, and has the necessary electrical, water, sink, drainage, and space requirements to perform the intended testing.

Process Location 2 (302/307 FAPC). After processing was performed in 228 FAPC (and even while it was ongoing), samples were transported to our microbiology laboratory or microbiology processing lab for microbial sampling (Phase 1) or for thermal sanitation of cores, followed by blending, incubation, and final microbial sampling (Phase 2). Rms 302/307 FAPC are also BSL-2 designated labs. Rm 307 FAPC is a traditional microbiology lab with autoclave, benches, incubators where microbial dilutions/plating is performed; 302 FAPC is a 'pathogen processing pilot plant' that is often used for processing of pathogen-inoculated samples for evaluation of thermal or chemical antimicrobial intervention. Both labs are adjoining to facilitate microbial plating when inoculated samples are handled/processed in the pathogen lab.

Protocols & Results: Phase 1.

Cultures. Bacterial cultures used in this study included *E. coli* O157:H7 PMM53150, ATCC 43890 (California outbreak isolate from human feces), ATCC 43894 (Michigan outbreak isolate from human feces), and ATCC 43895 (hamburger isolate implicated in human outbreak). Resistant variants of each strain was recovered to both Rifamycin S/V (10 ug/ml) and Gentamycin (10 ug/ml) whereby they were selectively recovered from non-sterile sample/meat environments in the presence of indigenous microbial backgrounds by plating on media containing these antibiotics.

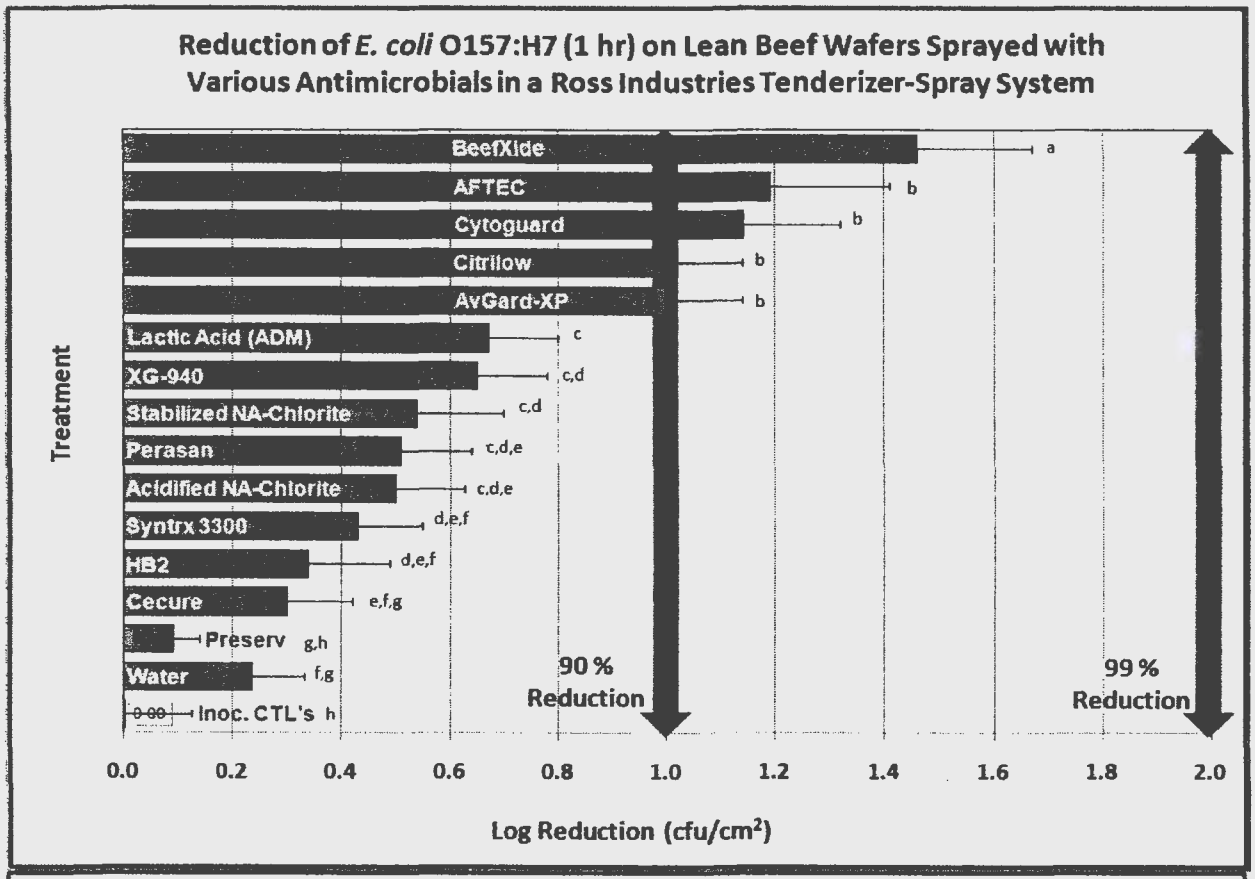
Assessment of antimicrobial spray treatment efficacy using lean sirloin wafers. We obtained numerous 'lean beef discs' from beef sirloins using a 2-inch diameter drill bit to 'core' a circular core from intact beef. Individual beef wafers, or discs (i.e., 20.25 cm^2), were then sliced from the cores for subsequent inoculation (~1 x 10^6 cfu/cm^2), 30 min holding, and then spray treatment with water or antimicrobials. Un-inoculated controls were also tested against our selection media as well as inoculated, but un-treated, samples that served as the basis of our microbial inoculation baseline. Samples inoculated and spray treated were kept on ice or refrigerated and processed for residual microbial counts. All samples were eventually stomached with DE Neutralizing broth and dilutions made in 0.1% buffered peptone water for plating. Samples not plated immediately after processing were held in bags in the refrigerator and then DE Neutralizing broth was added prior to microbial processing.

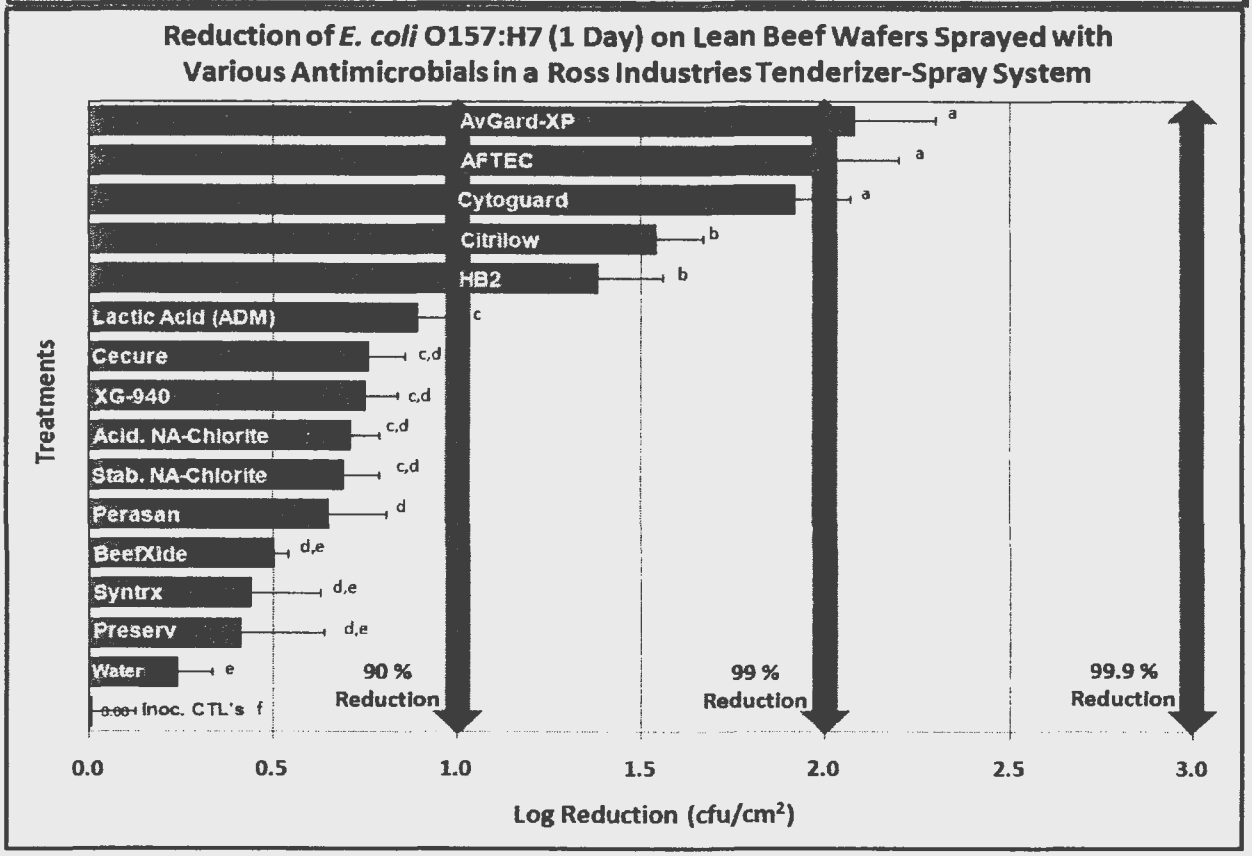
Sampling times:
a. 1 hr, as soon as possible after spray treatment (18 samples)
b. 1 day (18 samples)
c. 7 days(18 samples)
d. 14 days (18 samples)

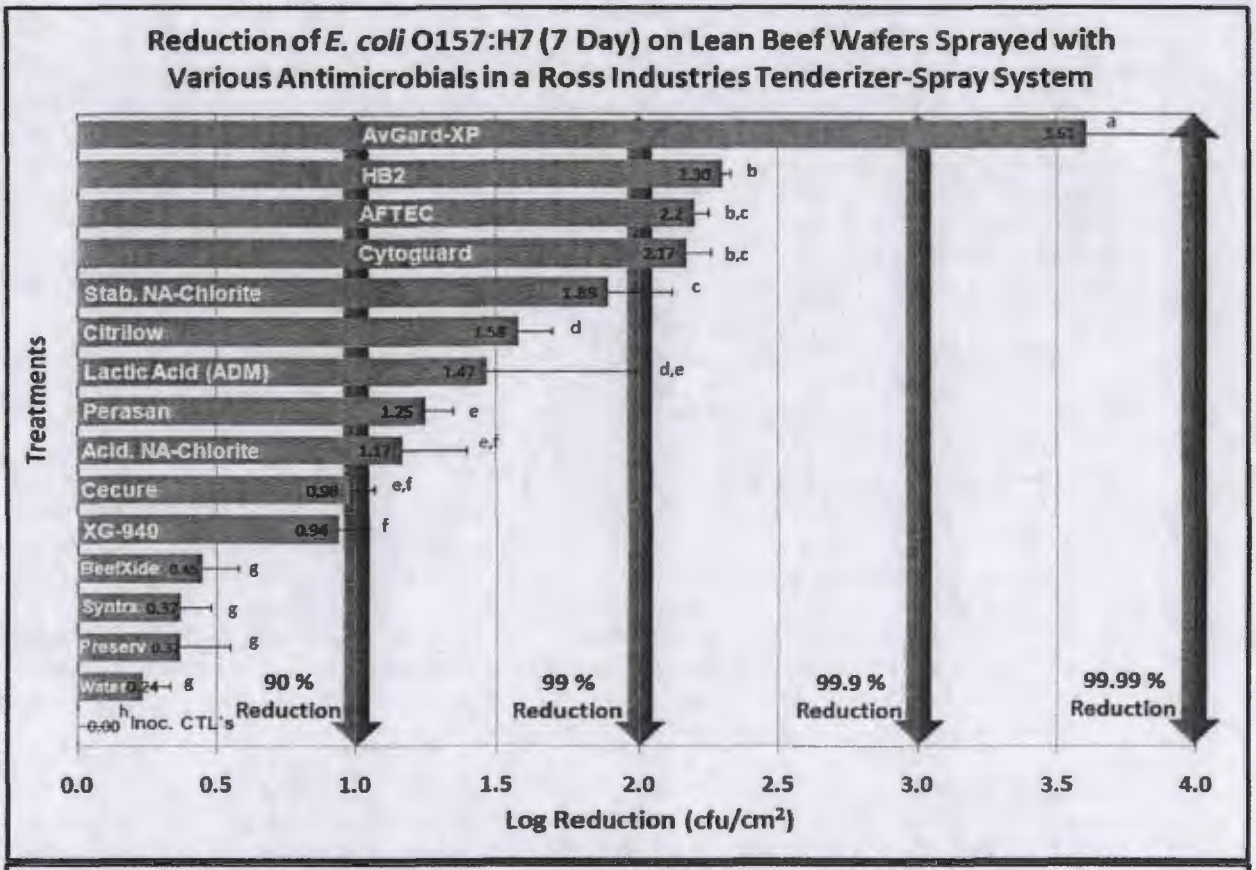
List of Antimicrobials Used in Phase 1

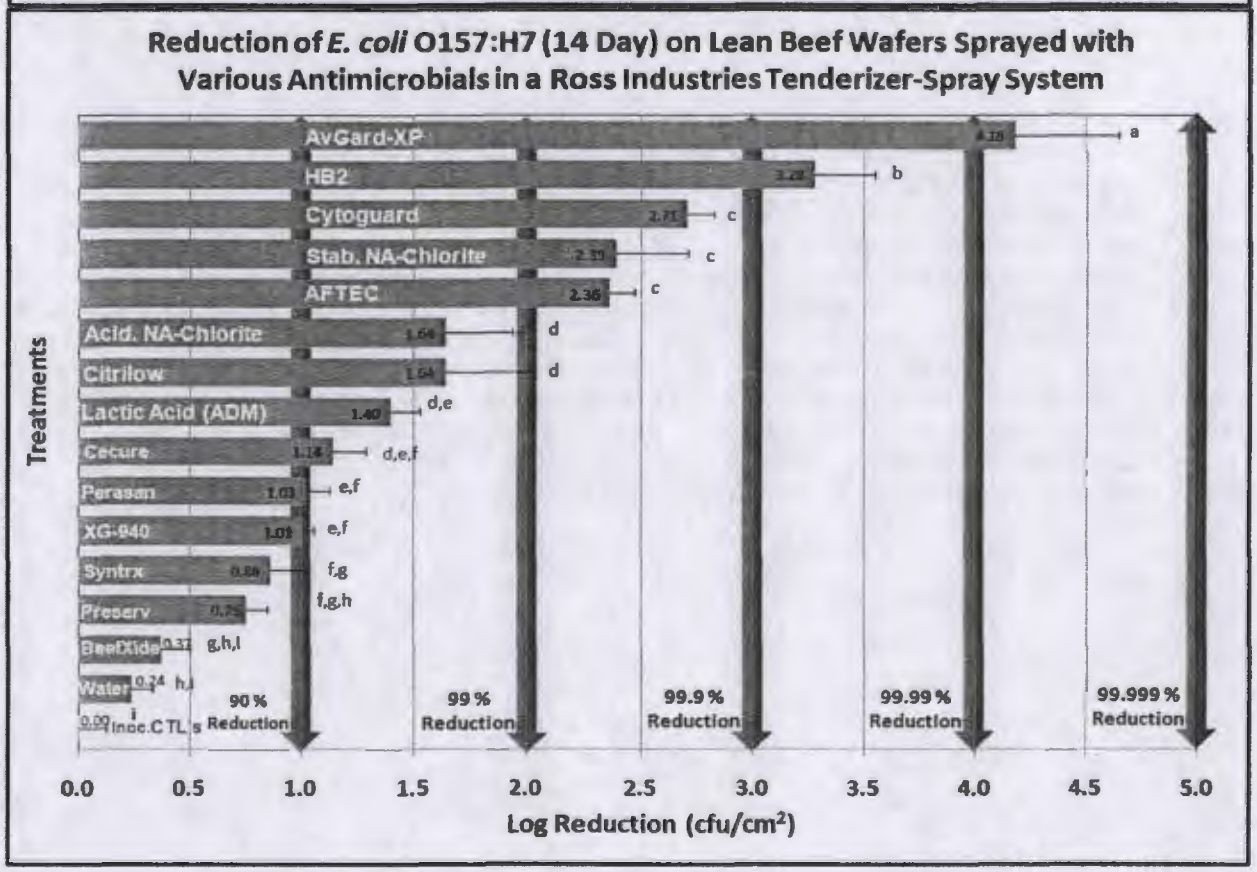
	Trade Name	Active(s)	pH	Application Strength
1.	AvGard-XP	Disodium Metasilicate	13.1	60,000 ppm SMS
2.	HB2	Hydrobromic Acid	7.5	300 ppm Br
3.	Cecure	Cetylpyridinium Chloride	7.0	4,000 ppm
4.	Preserv	Copper Sulfate Pentahydrate	6.8	*30% dilution of concentrate
5.	Stabilized Na Chlorite	Na Chlorite/Citric Acid/Na Hydroxide	6.5	*<1%, <1%, <1% each
6.	XG-940	Acidified Sodium Chlorite	6.5	200 ppm
7.	Perasan MP2	Peroxyacetic Acid	3.2	220 ppm
8.	Cytoguard PLUS	Lauric Arginate & Peroxyacetic Acid	3.0	5,000 ppm LAE; 220 ppm PAA
9.	Acidified Na Chlorite	Na Chlorite acidified with Citric Acid	2.7	1,100 ppm
10.	BeefXide	Lactic and Citric Acids	2.1	*2.4% dilution of concentrate
11.	Lactic Acid	Hydroxypropanoic Acid	1.9	50,000 ppm LA
12.	Syntrx 3300	HCl and Citric Acids	1.2	*3% dilution of concentrate
13.	AFTEC 3000	Buffered Sulfuric Acid	1.0	17,500 ppm
14.	Citrilow	HCl and Citric Acids	0.8	*18% dilution of concentrate

***Note:** For proprietary reasons the actual concentrations have not been disclosed; the 'application strength' listed is the dilution level of the concentrate provided by the manufacturer or approximate level of active.


Reduction of E. coli O157:H7 (1 hr) on Lean Beef Wafers Sprayed with Various Antimicrobials in a Ross Industries Tenderizer-Spray System
Treatment
BeefXide a
AFTEC b
Cytoguard b
Citrilow b
AvGard-XP b
Lactic Acid (ADM) c
XG-940 c,d
Stabilized NA-Chlorite c,d
Perasan c,d,e
Acidified NA-Chlorite c,d,e
Syntrx 3300 d,e,f
HB2 d,e,f
Cecure e,f,g
Preserv g,h
Water f,g
0.00 Inoc. CTL's h
90 % Reduction
99 % Reduction
0.0 0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6 1.8 2.0
Log Reduction (cfu/cm²)


Reduction of E. coli O157:H7 (1 Day) on Lean Beef Wafers Sprayed with Various Antimicrobials in a Ross Industries Tenderizer-Spray System
Treatments
AvGard-XP a
AFTEC a
Cytoguard a
Citrilow b
HB2 b
Lactic Acid (ADM) c
Cecure c,d
XG-940 c,d
Acid. NA-Chlorite c,d
Stab. NA-Chlorite c,d
Perasan d
BeefXide d,e
Syntrx d,e
Preserv d,e
Water e
0.00 Inoc. CTL's f
90 % Reduction
99 % Reduction
99.9 % Reduction
0.0 0.5 1.0 1.5 2.0 2.5 3.0
Log Reduction (cfu/cm²)


Reduction of E. coli O157:H7 (7 Day) on Lean Beef Wafers Sprayed with Various Antimicrobials in a Ross Industries Tenderizer-Spray System
Treatments
AvGard-XP
HB2
AFTEC
Cytoguard
Stab. NA-Chlorite
Citrilow
Lactic Acid (ADM)
Perasan
Acid. NA-Chlorite
Cecure
XG-940
BeefXide
Syntrx
Preserv
Water
Inoc. CTL's
90 % Reduction
99 % Reduction
99.9 % Reduction
99.99 % Reduction
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
Log Reduction (cfu/cm²)


Reduction of E. coli O157:H7 (14 Day) on Lean Beef Wafers Sprayed with Various Antimicrobials in a Ross Industries Tenderizer-Spray System
Treatments
AvGard-XP
HB2
Cytoguard
Stab. NA-Chlorite
AFTEC
Acid. NA-Chlorite
Citrilow
Lactic Acid (ADM)
Cecure
Perasan
XG-940
Syntrx
Preserv
BeefXide
Water
Inoc.CTL's
90 % Reduction
99 % Reduction
99.9 % Reduction
99.99 % Reduction
99.999 % Reduction
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
Log Reduction (cfu/cm²)

Discussion. The data obtained for the various antimicrobials demonstrated differences in microbial reduction of *E. coli* O157:H7 for both short-term and longer-term sampling intervals. Although the short term intervals may be more relevant to blade tenderization, the longer-term intervals could provide information for applications whereby products may be sprayed, packaged, and then delivered to final use sources (i.e., the reduction is obtained during transportation/storage before use). It is also not clear if the longer-term intervals may apply to *E. coli* O157:H7 that could become translocated into blade channels in beef along with the respective antimicrobial, thereby eliciting a reduction over time *internally.* In hindsight, it was also apparent that antimicrobials (some which were similar to others, and some that were not), were applied at respective use levels specified by each manufacturer as opposed to targeting a specific concentration (and not all concentrations in the supplied solutions were openly identified). So in that respect, comparisons can only be made for the use level specified (by the manufacturers), some concentrations were not identified due to 'proprietary reasons' and likely resulted in different concentrations of similar agents provided by the different suppliers. In one instance, two similar actives were tested from different suppliers: Acidified Sodium Chlorite (+citric acid; 1,100 ppm) gave slightly better results than XG-940 (200 ppm acidified sodium chlorite) during the longer hold time, which can be attributed to the higher concentration of ASC used and possibly because of the citric acid in the blend used to acidify the product. Additional studies with any respective supplier may be needed to investigate enhancement of reduction levels different from those obtained in this study, since the nature of this study was simply a one-off testing and not an optimization for any given antimicrobial. Initially, I (Dr. Muriana) was under the assumption that we were only going forward with the best 2-3 antimicrobials into Phase 2, but subsequently that was broadened at the suggestion of Dr. Morgan/Wayne Spillner into the best 7 (of the 14) from the 7-day data that would proceed forward into Phase 2. This would give a larger evaluation for half of the antimicrobials examined in Phase 1 and accommodate more sponsors than was originally intended for Phase 2.

Phase 1 determined the efficacy of reduction of *E. coli* O157:H7 on the surface of lean beef discs as would occur if the *E. coli* were on the surface of beef subprimals. The reasoning is that reduction of the surface bacteria by the antimicrobial(s) reduces the chances for translocation (internalization) during blade tenderization. However, solution strengths that can be used commercially are limited by federally-approved limits for specific compounds (i.e., FDA-approved for foods based on safety, and USDA-FSIS approved for meat and poultry products based on efficacy) as well as costs, but spray dosage levels can be modified. Another factor that can play an important role to enhance the effect of antimicrobials is the solution temperature that is applied. In our study, we examined solutions applied at room temperature to comply with the least complicated, and likely, the most prevalent commercial situation. However, solutions applied at warmer temperatures may provide better access of the antimicrobials to the surface bacteria (bacteria may be protected by fatty film on the surface of meats at room temperature) and/or enhance their lethality by short-term temperature-enhanced inhibition. Other approaches that are yet to be examined include combinations of antimicrobials, although some of which have already been included in this study, such as Cytoguard PLUS (lauric arginate + peroxyacetic acid) which outperformed peroxyacetic acid alone in this study. There is still the possibility that those antimicrobials that were not chosen for Phase 2, could still perform sufficiently well for commercial applications given attention to details that were not examined in this study: different concentration, application temperature, and/or possible synergistic effects when applied in combination with other antimicrobials that have different modes of action.

Protocols & Results: Phase 2.

Cultures. The *E. coli* O157:H7 cultures were the same as those used in Phase 1 and were handled similarly (freshly grown for the morning of use, washed, inoculated and allowed 30-min attachment time before proceeding with treatments).

Beef subprimals. Beef subprimals were obtained fresh from a local processor, the day prior to use and the cap was removed for Phase 2 so that a contiguous intact core could be obtained.

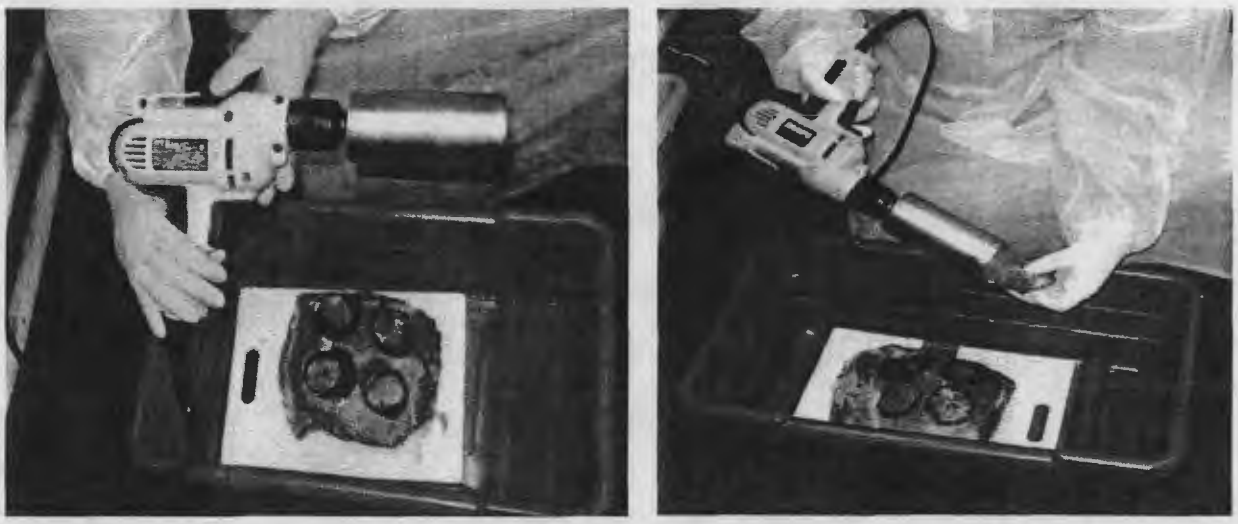
Inoculation of subprimals. Beef samples were inoculated by marking a circle on the surface of the beef suprimals with an imprint using edible ink that was a smaller diameter than our 2-inch coring device. After inoculation (~ 1.0×10^4 cfu/cm^2), samples were allowed a 30-min attachment time. Several regimens were utilized for each antimicrobial solution:

a) Inoculation, water spray (no blade treatment), and core removal,
b) Inoculation, water spray, blade tenderization, and core removal,
c) Inoculation, antimicrobial spray, blade tenderization, and core removal.

Phase 2 Antimicrobials

Trade Name	Active Ingredient(s)	Application Strength	pH
AvGard-XP	Disodium Metasilicate	60,000 ppm SMS	13.1
HB2	Hydrobromic Acid	300 ppm Br	7.5
Stabilized Na Chlorite	Na Chlorite/ Citric Acid/Na Hydroxide	*<1%, <1%, <1% each	6.5
Cytoguard PLUS	Lauric Arginate & Peroxyacetic Acid	5,000 ppm LAE; 220 ppm PAA	3.0
Lactic Acid (FCC 88%)	Hydroxypropanoic Acid	50,000 ppm	1.9
AFTEC 3000	Buffered Sulfuric Acid	17,500 ppm	1.0
Citrilow	Hydrochloric & Citric Acids	*18% dilution of concentrate	0.8

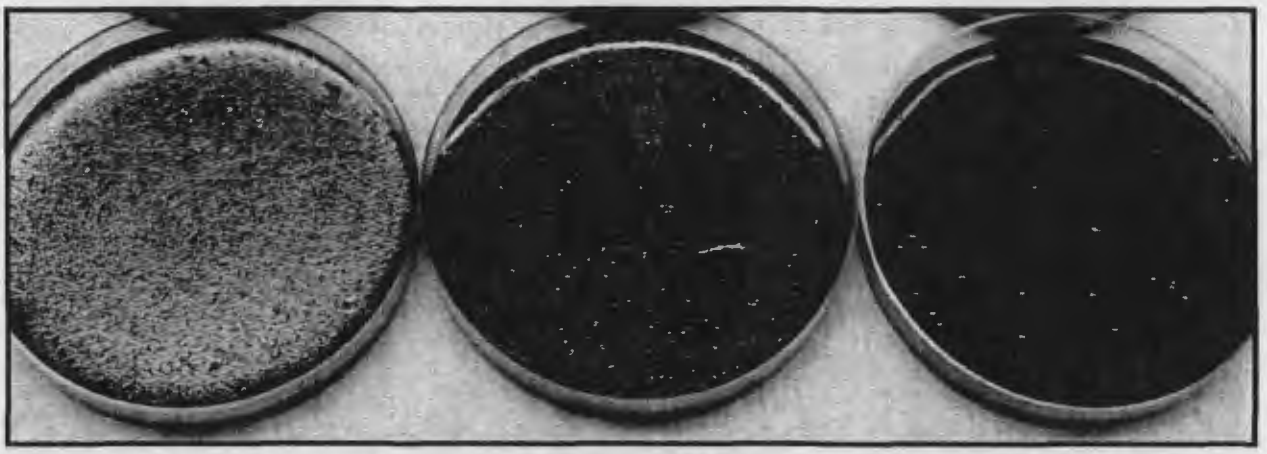
***Note:** For proprietary reasons the actual concentrations have not been disclosed; the 'application strength' listed is the dilution level of the concentrate provided by the manufacturer or approximate level of active.



Drill and 2-inch diameter circular drill bit used to excise core samples from inoculated, sprayed, and blade-tenderized subprimals.

Core sample recovery. After exiting the Ross Integrated Tenderizer, beef cores were obtained using a 2-inch circular drill bit along the inoculated surface areas. In order to eliminate confusion of the source of the microbes after blending and plating (i.e., whether they were translocated internally or were from the core-surface contamination), we took several steps to eliminate non-translocated contaminants from the core surface. The ¼-inch of the inoculated surface of the cores was cut off after coring.

To further eliminate surface contamination from recovered beef cores we used a radiant-heat oven (i.e., IR Grill) to surface heat all post-treatment beef cores before sectioning and blending. Dr. Muriana has used IR Grill heating as a pre-package antimicrobial intervention for RTE meats that is accepted by USDA-FSIS as a post-process antimicrobial intervention. We used this same process to eliminate incidental contamination on the surface of the beef cores prior to sectioning, blending, and enrichment.



After careful aseptic sectioning (1-inch segments), individual core sections were blended in a minimal volume (2:1) of enrichment broth and incubated for 1 day at 30°C. After incubation, 1-ml of the blended samples was then extracted with *E. coli* O157:H7-specific immunomagnetic beads (i.e., magnetic beads coated with antibodies specifically to *E. coli* O157:H7). This allowed selective recovery by use of immunomagnetic beads that was facilitated by an automated 'Bead Retriever'. The entire amount of recovered magnetic beads after extraction of the 1-ml enrichment sample was plated onto EMB agar containing Rifamycin (to which our inoculated strains were resistant). This provided selective recovery by antibodies (beads), selective recovery by antibiotic resistance (plates), and differential detection (green sheen of colonies) of *E. coli* O157:H7 from EMB-Rif agar for our positive samples. Negative samples did not have the green sheen or did not have any colonies.

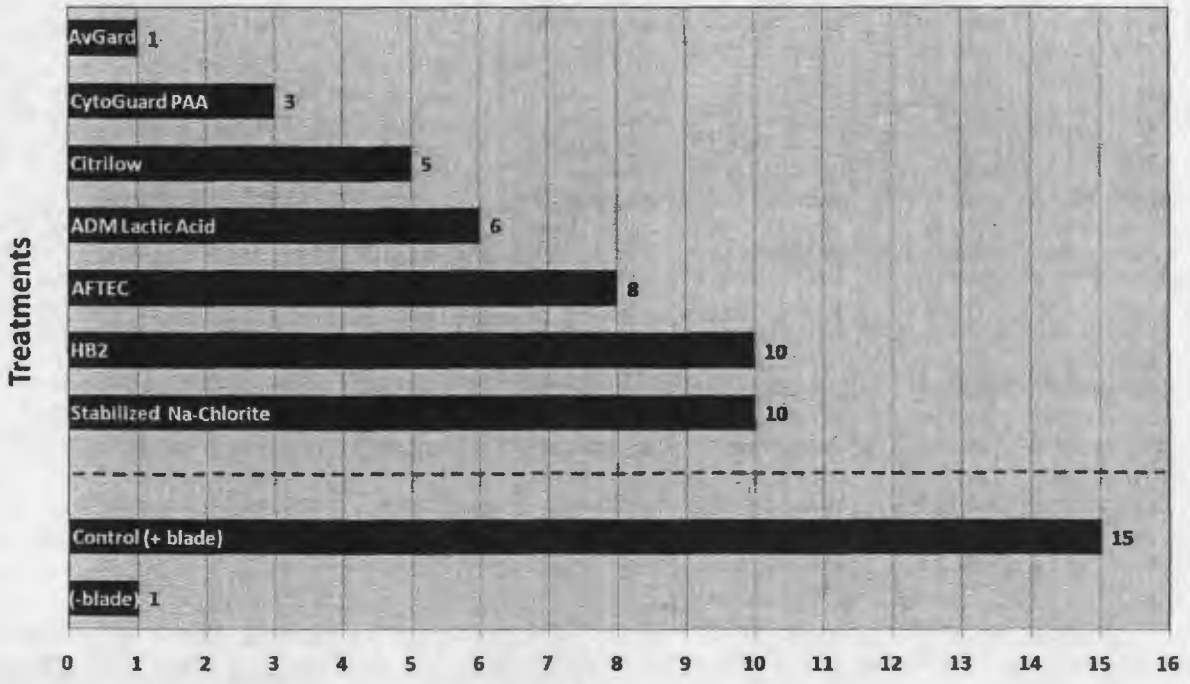
Appearance of *E. coli* O157:H7 on CT-SMAC agar.

We first examined the possibility of using CT-SMAC (Sorbital-MacConkey Agar + cefixime & tellurite) as the selective media for *E. coli* O157:H7, however, the colonies were very pale and not distinctive, and after extended incubation changed color a bit. Since this part of our process was not heavily dependent on the medium for selection from a diverse background flora as occurs during ground beef testing (i.e., the broth enrichment followed by immunomagnetic bead enrichment gave us overhwelming levels of our *E. coli* O157:H7 recovered), we decided to use EMB medium containing one of the antibiotics for which the strains were resistant to as a positive visual score for Rifamycin-resistant *E. coli*. All of our EMB-Rifamycin plates for Phase 2 had in excess of 1,000 colonies or higher and the 'green sheen' was an easy visual score for presence after the double enrichment (broth medium & immunomagnetic bead recovery using 1-ml of enrichment broth, wash, and plating).

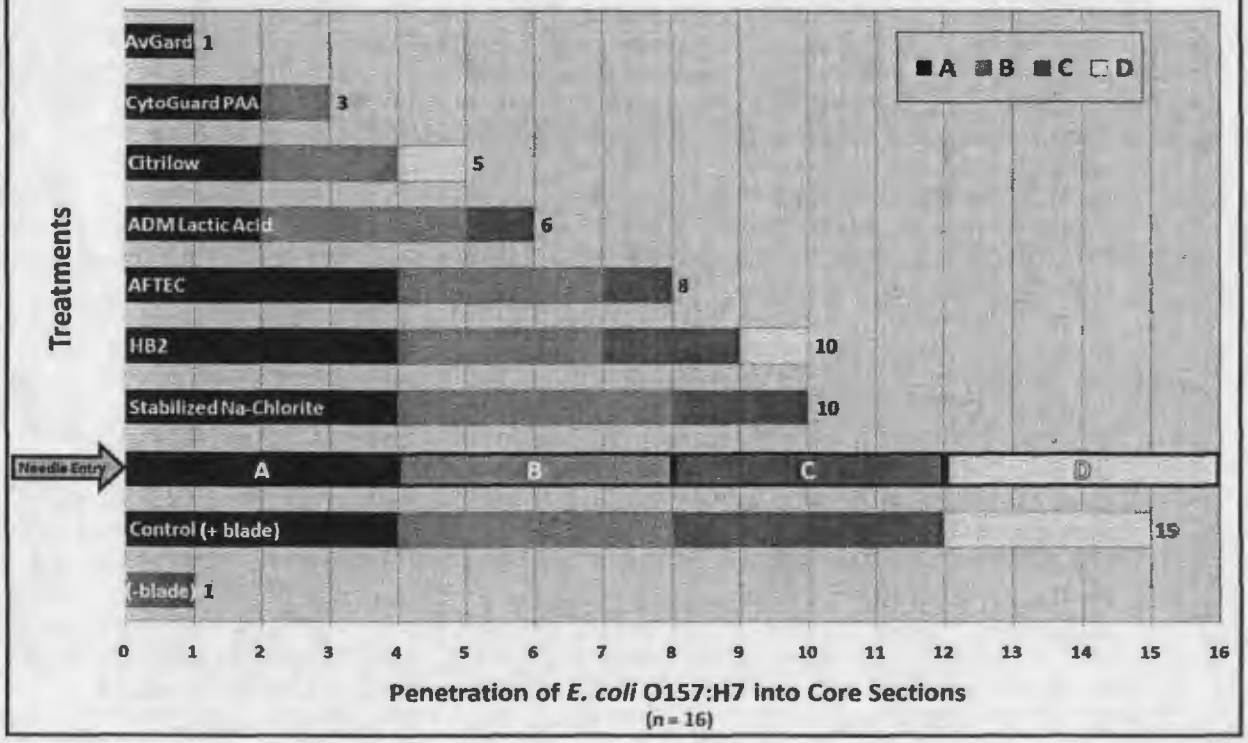
For each antimicrobial tested, we obtained 4 core samples, each sectioned into 4 sections. Results were tabulated as total sections positive per core as well as sections positive for each depth penetration that the sections represented (1-, 2-, 3-, 4-inches).

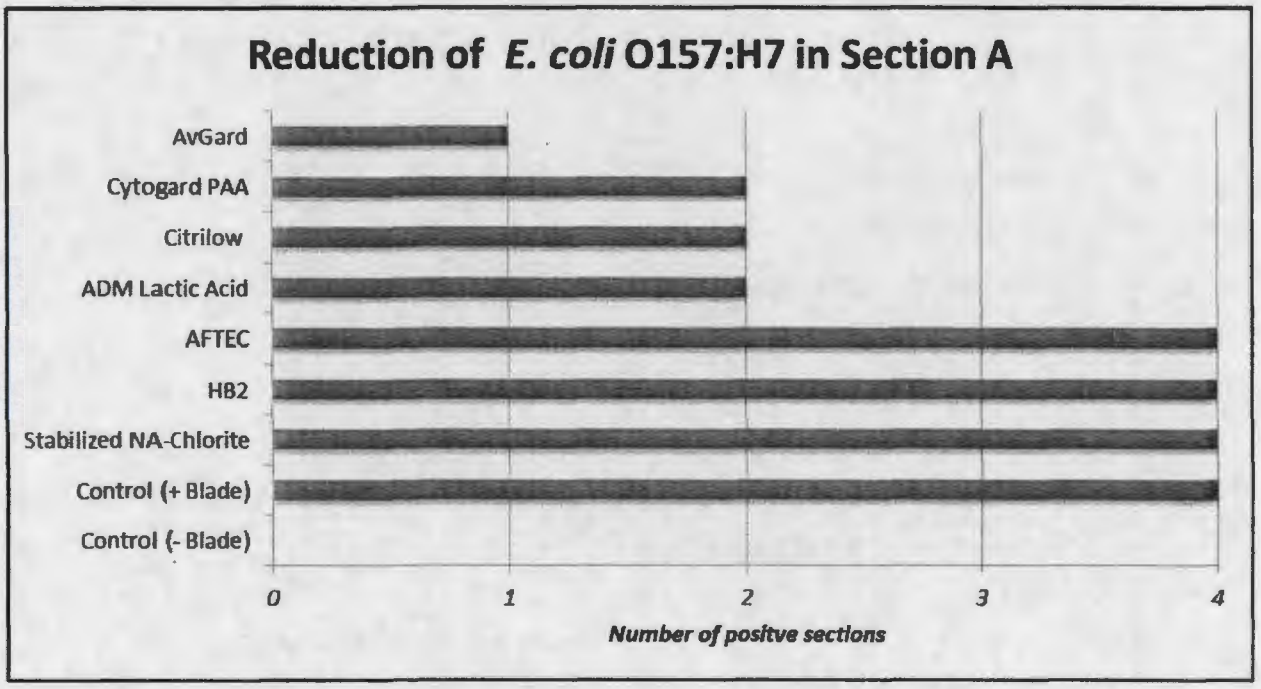
Discussion. The data obtained shows that all antimicrobial interventions reduced the number of segments containing *E. coli* O157:H7 relative to controls (top graph). Some interventions were more efficacious then others (at the levels used). The antimicrobials showing lower efficacy could likely be improved with further testing and tweaking, however this study did not provide that opportunity. As we look as the *E. coli* O157-H7-positive samples within each depth interval, it appears that as antimicrobials were more effective in reducing the number of sections that were positive, the sections that were being eliminated were those that were deeper. For instance, *E.* coli-positive samples were only recovered from the top-most 1-inch of penetration with AvGard which demonstrated the greatest efficacy. As efficacy increased, *E. coli* O157 was eliminated from the deeper depths in meat samples.

Phase 2 Results: Reduction of *E. coli* O157:H7 in Beef Core Sections after Inoculation, Spray Treatment, and Blade-Tenderization

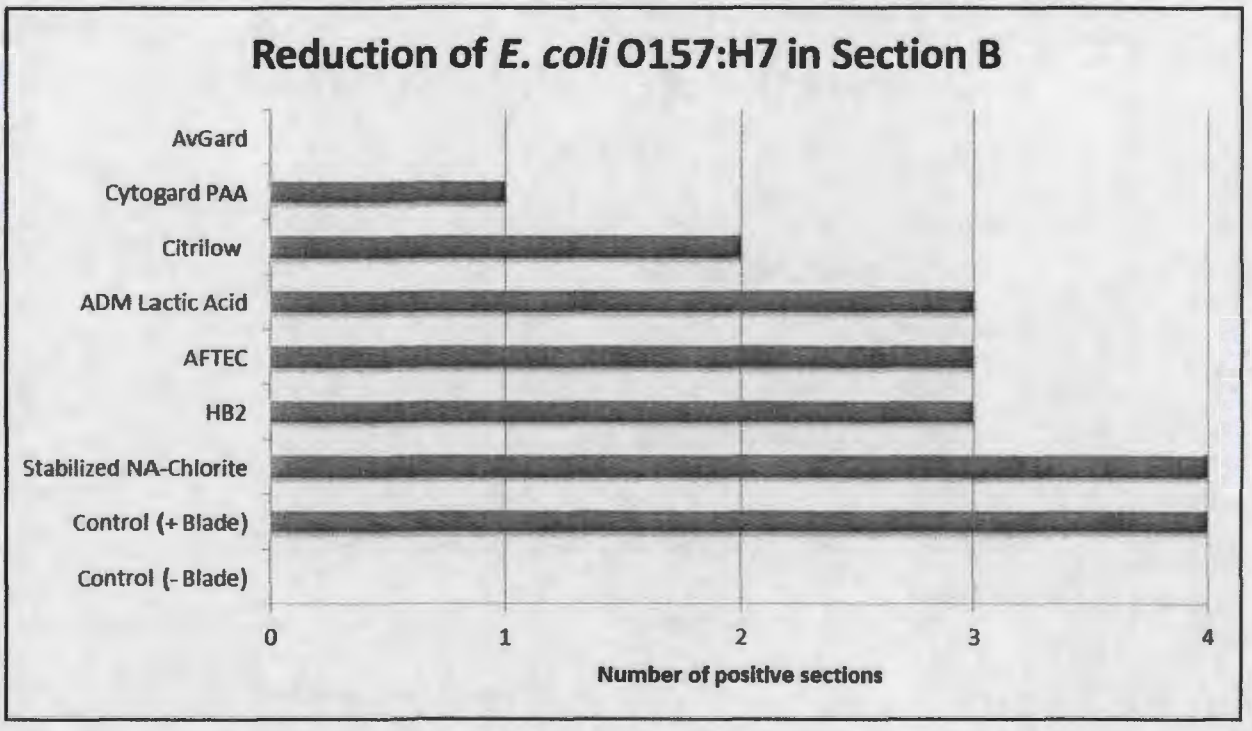


Phase 2 Results: Penetration of *E. coli* O157:H7 into Beef Core Sections after Inoculation, Antimicrobial Spray, and Blade Tenderization

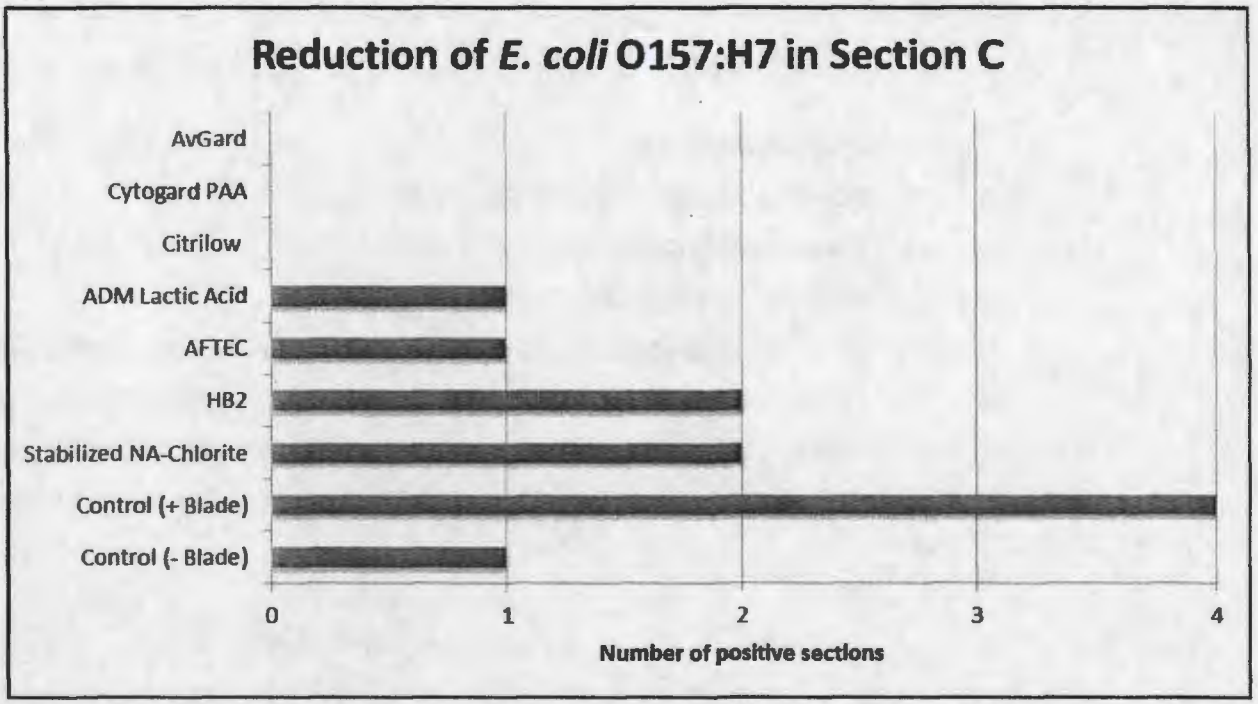




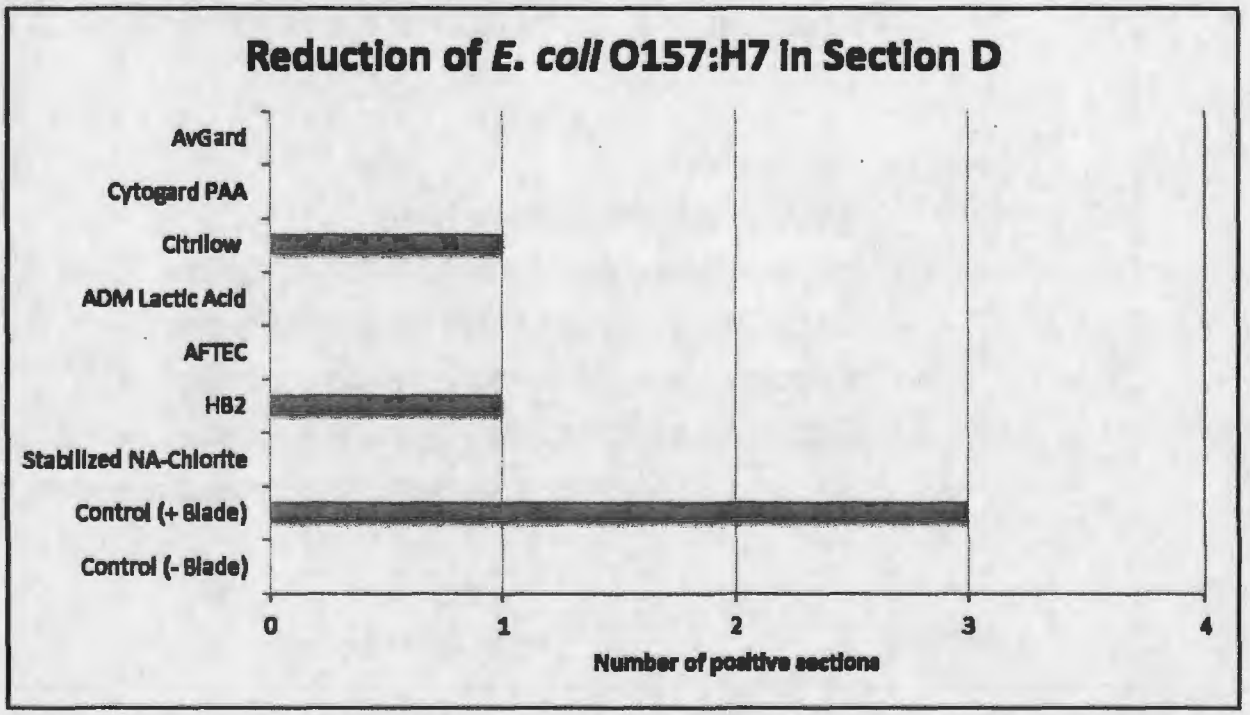
Section A. Recovery of *E. coli* O157:H7 from the top-most 1-inch inoculated side of the beef core. *E. coli* O157:H7 was recovered from all 4 control (+blade) sections, AFTEC, HB2, and Stabilized Na-Chlorite; from only 2 sections treated with Cytoguard PLUS, Citrilow, and Lactic Acid; and from only 1 section treated with AvGard-XP.



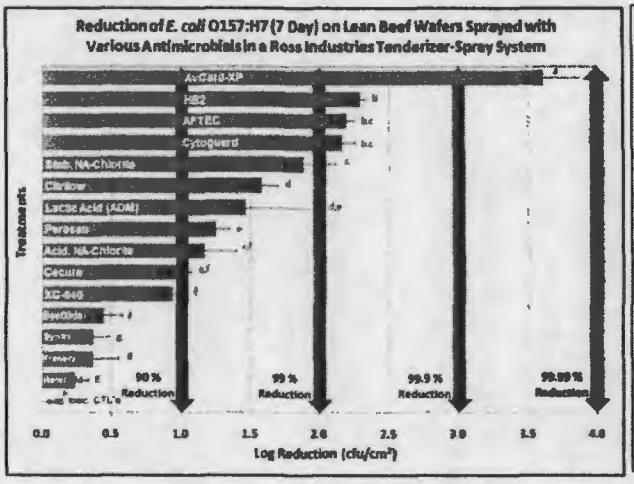
Section B. Recovery of *E. coli* O157:H7 from the second 1-inch layer of beef cores. *E. coli* O157:H7 was recovered from all 4 control (+blade) sections and Stabilized Na-Chlorite; from only 3 sections treated with Lactic Acid, AFTEC, and HB2; from 2 sections treated with Citrilow; and from only 1 section treated with Cytoguard PLUS, *E. coli* O157:H7 was not recovered from sections at this level when treated with AvGard-XP.

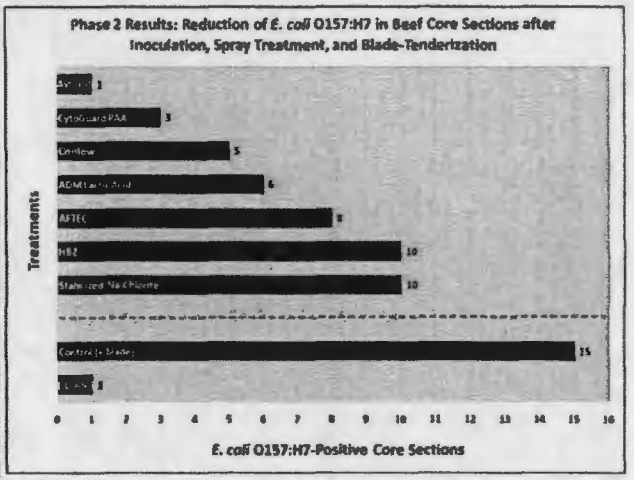


Section C. Recovery of *E. coli* O157:H7 from the 3-inch layer of beef cores. *E. coli* O157:H7 was recovered from all 4 control (+blade) sections but from only 2 sections when treated with Stabilized Na-Chlorite or HB2; from only 1 section when treated with Lactic Acid or AFTEC; *E. coli* O157:H7 was not recovered from this level when treated with Citrilow, Cytoguard PLUS, or AvGard-XP. *E. coli* O157:H7 recovered from 1 non-bladed control section, presumably due to external contamination.



Section D. Recovery of *E. coli* O157:H7 from the bottom (4-inch) layer of beef cores. *E. coli* O157:H7 was recovered from 3 of 4 control (+blade) sections and from only 1 section treated with Citrilow or HB2; no *E. coli* were recovered from this lowest section when treated with Stabilized Na-Chlorite, AFTEC, Lactic acid, Cytoguard PLUS, or AvGard-XP.





The two Phases of this study are somewhat different, yet are complimentary to each other.

Phase 1 deals with the application of an antimicrobial onto *E. coli* O157:H7 surface-inoculated beef discs and quantification of survivors to determine reduction of initial population on the surface.

Phase 2 also uses surface-inoculated beef discs that are sprayed with antimicrobials, but is different in that we perform blade tenderization and look for recovery of internalized *E. coli* which is proportional to the reduction of *E. coli* O157:H7 on the surface (i.e., the greater the reduction on the surface, the less likely you will recover it from internalized sections after blade tenderization). That is, you need a sufficiently high population on the surface to observe translocation to internal sections.

The data obtained in Phase 2 compliments that which was obtained in Phase 1 based on performance. For instance, AvGard-XP was shown in Phase 1 to have the greatest reduction of *E. coli* O157:H7 on lean beef discs (7-days) and similarly, in Phase 2 gave the fewest *E. coli* O157:H7-positive samples (only 1 of 16) in Phase 2 testing. This strongly confirms the efficacy of AvGard-XP as an antimicrobial in both types of testing. Phase 2 testing also complimented Phase 1 results with other antimicrobials. Cytoguard PLUS was close to 2nd (not significantly different) in Phase 1 and was 2nd in efficacy in Phase 2 (Cytoguard PLUS)

Conclusion: The use of antimicrobial spray interventions prior to blade tenderization (i.e., integral solution intervention) can reduce the population of *E. coli* O157:H7 to lower levels than those that occur prior to spray treatment, and therefore, can reduce the likelihood of translocation to beef internal sections concomitant with lower surface populations. The novelty of antimicrobial intervention as demonstrated herein, may be applied immediately prior to blade tenderization (Phase 2 data) or perhaps even further upstream in the sourcing process as our Phase 1 data demonstrated antimicrobial efficacy at 1 & 2 week holding time.

Additional Research: The data obtained for Phase 2 is certainly positive, but is limited in the amount of data generated for any one antimicrobial. We would need to establish greater degree of confidence by providing more detailed examination of which ever supplier would like to pursue additional, in-depth testing with their antimicrobial(s), including possible synergism with oxidative water solutions, different temperature of application, and/or different concentrations.

Attachment 8

Study title: Antimicrobial treatment of beef trimmings for control of *Escherichia coli* O157:H7 and *Salmonella spp.* using a Sulfuric Acid/Sodium Sulfate blend (Aftec)

Conducted by: James L. Marsden, Ph.D., Regent's Distinguished Professor—Food Safety & Security, Kansas State University

Study dates: October 2009

Objective: to establish the efficacy of treatment using Aftec on beef trimmings for control of *E. coli* O157:H7 and *Salmonella*. Also, evaluate effect on shelf life, color, and residues.

Methodology: Beef trimmings inoculated with a 5-strain cocktail of *E. coli O157:H7 or Salmonella* spp. were sprayed with a solution of *Aftec* adjusted to a pH of 1.3-1.5 for periods of 0, 10, 20 and 30 seconds. The target surface inoculation was 7.0 Log CFU/cm^2 . After each treatment, the trimmings were tested to determine reductions of each pathogen tested. Three replications were conducted. For sensory evaluation, ground beef manufactured using beef trimmings treated with Aftec at 10, 20, and 30 second time intervals were compared to a control in triangle tests using a trained sensory panel. Chemical tests were conducted for residuals.

Results and discussion: The 10 second treatments for pathogens *E. coli* O157:H7 and *Salmonella* spp. showed 0.7 and 1.1 Log CFU/cm^2 reductions, respectively. The highest lethality was achieved with the 30 second treatments for both pathogens, *E. coli* O157:H7 and *Salmonella* spp., which showed 1.5 and 1.6 Log CFU/cm^2 reductions, respectively.

The study conducted a sensory evaluation comparing a control to ground beef manufactured using beef trimmings treated with AFTEC at 10, 20, and 30 second time intervals in triangle tests using a trained sensory panel. No differences between the treated samples and the control were reported.

The study also examined the shelf life of treated products. Samples were evaluated daily for visual color and microbiological testing for total aerobic plate count. No differences in color stability were observed between treated samples versus the control. No significant differences in aerobic plate counts were reported between treated and control ground beef samples. Finally, no statistical differences in residual levels of sodium sulfate or sulfuric acid were reported in ground beef treated with the Aftec solution versus control samples. This would support the categorization of the treatments using Aftec as a processing aid.

Antimicrobial treatment of beef trimmings for control of *Escherichia coli* O157:H7 and *Salmonella* spp. using a Sulfuric Acid/Sodium Sulfate blend (*Aftec*)

Final Report

October 13, 2009

Submitted to:
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Introduction:

The control of *E. coli* O157:H7 and *Salmonella* in beef trimmings is essential for the production of safe ground beef products. An integrated food safety system for ground beef involves the application of control measures during the slaughter process and at other critical points in the process. An effective intervention applied to beef trimmings prior to grinding would provide an important reduction in risk. The evaluated chemistry in this study is a Sulfuric Acid/Sodium Sulfate blend adjusted to a pH of 1.3-1.5. The brand name for this product is *Aftec* and it is manufactured by Advanced Food Technologies, LLC. The ingredients are FDA GRAS and use of product as an acidifier has already been approved by USDA FSIS for meat and poultry applications. The purpose of this study was to establish the efficacy of treatment using *Aftec* on beef trimmings for control of *E. coli* O157:H7 and *Salmonella.*

An advantage of this approach is the ease of application and availability to small processors. The make-up of the antimicrobial solution and application can be conducted in operations of any size. Since the anti-microbial effect is not due to oxidation, it can be easily applied without adversely affecting the quality of the trimmings or ground beef manufactured from treated trimmings.

This study involved a spray application of *Aftec* at various durations on beef trimmings. Future studies will evaluate the efficacy of dipping applications and other methods of applying the product in various meat processing steps.

This study was designed to measure the effect of the treatment on ground beef shelf life, color, sensory characteristics and residues in order to support a request to USDA's Food Safety and Inspection Service that treatment of beef carcasses, beef subprimals and beef trimmings using Aftec would be considered as an anti-microbial use.

The beef industry and FSIS share the objective of reducing the risk of E. coli 0157:H7 and Salmonella in raw ground beef. The availability of effective interventions that may be applied at appropriate processing steps is essential to meeting that objective.

Materials and Methods

Bacterial Culture Preparation: The following strains from the Kansas State University culture collection were used to prepare the inoculum:

- *Escherichia coli* O157:H7: ATCC 43890 and ATCC 43889, obtained from Jackie Staats at KSU Veterinary School; USDA-FSIS 380-94, KSU 01, CDC (Patient outbreak), and KSU 03, CDC (Meat outbreak).
- *Salmonella* spp.: *Salmonella choleraesuis* subsp. *cholerasuis (S. enteriditis) (ATCC 4931,* and USDA-FSIS 15060*), S. seftenburg* subsp. *cholerasuis* (ATCC 43485), *S. newport* (Dr. Phebus, KSU), and *S. montevideo* (Dr. L. Beuchat, UGA).

To prepare the inoculum, stock cultures were cultivated by placing one impregnated bead into a 5 ml solution of Difco® Tryptic Soy Broth (TSB) and incubating for 24 h at 35°C. Next, a 0.05 ml loop of the respective culture was inoculated into a 10 ml solution of TSB and incubated for 24 h at 35°C. All five samples from each culture were mixed together to create a 50 ml cocktail containing 10^9 to 10^{10}CFU/ml of *E. coli* O157:H7 or *Salmonella* spp. The cell density of this suspensions was determined by plating appropriate dilutions on MSA (MacConkey Sorbitol Agar, Difco, Detroit, MI) for *E. coli* O157:H7 and XLD (Xylose Lysine Desoxycholate Agar, Difco, Detroit, MI) for *Salmonella* spp., and placed in the incubator for 48 hours at 35°C. Cultures were confirmed by cultivation on selective and differential media, and biochemical analysis of presumptive colonies using API 20E kits.

Sample Preparation: Beef trimmings were obtained from the KSU meat laboratory and cut into app. one inch square pieces. The trimmings were held at 40°F prior to treatment. Selected trimmings were inoculated with *Escherichia coli* O157:H7 or *Salmonella* spp. inside a "bio-containment" chamber by "misting" the surface of the meat with approximately 10 ml of the inoculum. This was done ensuring that all sides of each piece of meat received the same exposure to the inoculum. Samples were held for 30 min at room temperature to allow proper bacterial attachment to the surface of the meat. Immediately prior to treatment applications, the surfaces of the inoculated products were sampled and analyzed to establish the actual inoculum level of the attached organisms.

Application of Treatment: Beef trimmings inoculated with a 5-strain cocktail of *E. coli O157:H7 or Salmonella* spp. were sprayed with a solution of *Aftec* adjusted to a pH of 1.3-1.5 for periods of 0, 10 20 and 30 seconds. The target surface inoculation was 7.0 Log CFU/cm^2. After each treatment, the beef trimmings were tested to determine reductions of each pathogen tested. Three replications were conducted for each treatment.

Sampling Method: Individual pieces of beef trimmings were placed into a stomacher bag. The tissue samples were diluted with 90 ml of 0.1% sterile peptone water (PW) and homogenized in a stomacher for one minute. Samples were serially diluted in sterile PW and plated onto corresponding media for each pathogen tested. The plates were incubated at 37 °C for 48 hrs. The colony forming units were enumerated and calculated as the difference in log recovery.

Sensory Evaluation: Ground beef manufactured using beef trimmings treated with Aftec at 10, 20, and 30 second time intervals were compared to a control in triangle tests using a trained sensory panel. No differences between the treated samples and the control were reported.

Shelf Life Determination: Ground beef manufactured using beef trimmings treated with Aftec at 0 (control), 10, 20, and 30 second time intervals were packaged in overwrap oxygen permeable packages and placed in a commercial display case for a period of 5 days. Samples were evaluated daily for visual color and microbiological testing for total aerobic plate count. No differences in color stability were observed between treated samples versus the control. The total aerobic plate counts are listed in Table 3. No significant differences in APC's were reported between treated and control ground beef samples.

Results and Discussion:

Results from this study can be found in Tables 1, 2 and 3. Log CFU/cm^2 reductions were calculated as the difference in log recoveries from the inoculated products prior to treatment and the log recovery after treatment.

Table 1. Average recoveries (Log CFU/cm^2) of *Salmonella* spp and *E. coli* O157:H7 in boneless beef trimmings treated with a solution of *Aftec* Sulfuric Acid and Sodium Sulfate blend (pH 1.3-1.5) for periods of 0, 10, 20 and 30 seconds.

Sample	*Salmonella*	*E. coli* O157:H7
Control (0 Seconds)	6.9	6.7
10 Seconds	5.8	6.0
20 Seconds	5.5	5.6
30 Seconds	5.3	5.2

Table 2 shows the average reductions obtained from the boneless beef trimmings sprayed with a solution of *Aftec* Sulfuric Acid and Sodium Sulfate blend (pH 1.3-1.5) for periods of 0, 10, 20 and 30 seconds. The highest lethality was achieved with the 30 seconds treatments for both pathogens, *E. coli* O157:H7 and *Salmonella* spp., which showed 1.6 and 1.5 log cfu/cm2 reductions, respectively.

Table 2. Average reductions (Log CFU/cm^2) of *Salmonella* spp and *E. coli* O157:H7 in boneless beef trimmings treated using *Aftec* Sulfuric Acid and Sodium Sulfate blend (pH 1.3-1.5) for periods of 10, 20 and 30 seconds.

Sample	*Salmonella* spp.	*E. coli* O157:H7
10 Seconds	1.1	0.7
20 Seconds	1.4	1.1
30 Seconds	1.6	1.5

Table 3. Aerobic Plate Counts during 5 days Shelf Life Storage in Ground Beef manufactured using beef trimmings treated using *Aftec* Sulfuric Acid and Sodium Sulfate blend (pH 1.3-1.5) for periods of 0 (control), 10, 20 and 30 seconds.

	Control	*10 Seconds*	*20 Seconds*	*30 Seconds*
Day 1	**1.9×10^3 cfu/gm**	**1.0×10^3 cfu/gm**	**1.3×10^3 cfu/gm**	**1.2×10^3 cfu/gm**
Day 2	**2.3×10^3 cfu/gm**	**1.8×10^3 cfu/gm**	**2.0×10^3 cfu/gm**	**2.1×10^3 cfu/gm**
Day 3	**3.1×10^3 cfu/gm**	**2.9×10^3 cfu/gm**	**3.0×10^3 cfu/gm**	**2.9×10^3 cfu/gm**
Day 4	**5.7×10^3 cfu/gm**	**5.1×10^3 cfu/gm**	**5.3×10^3 cfu/gm**	**5.3×10^3 cfu/gm**
Day 5	**5.9×10^3 cfu/gm**	**5.8×10^3 cfu/gm**	**5.5×10^3 cfu/gm**	**5.6×10^3 cfu/gm**

The results of this study demonstrate that the treatments using *Aftec* Sulfuric Acid and Sodium Sulfate blend (pH 1.3-1.5) at 10, 20 and 30 seconds were effective at reducing levels of *Salmonella* and *E. coli* O157:H7 on inoculated beef trimmings. The greatest reductions were achieved with the 30 second spray.

There was no long term residual effect on the color, shelf life, or microbiological quality of ground beef manufactured from the treated trimmings versus the control. In addition, no statistical differences in residual levels of sodium sulfate or sulfuric acid were reported in ground beef treated with the *Aftec* solution versus control samples. This would support the classification of *Aftec* as an anti-microbial and categorization of the treatments using Aftec as a processing aid.

SUBMISSION END

Appendix III: Proof of GRAS Notification

Agency Response Letter GRAS Notice No. GRN 000003

CFSAN/Office of Premarket Approval

June 5, 1998

Ms. Betty J. Pendleton
Jones-Hamilton Co.
15505 Country Ridge Drive
Chesterfield, MO 63017

Re: GRAS Notice No. GRN 000003
Docket No. 98S-0104

Dear Ms. Pendleton:

This is in response to your GRAS notice dated February 11, 1998, which was received by the Food and Drug Administration (FDA) on February 26, 1998. This request was submitted to FDA on behalf of Jones-Hamilton Co. in accordance with the agency's proposed regulation, proposed 21 CFR 170.36 (62 FR 18938; April 17, 1997). FDA designated your notice as GRAS Notice No. GRN 000003.

Your notice states that Jones-Hamilton Co. has determined that sodium bisulfate ($NaHSO_4$; CAS Reg. No. 7681-38-1) is generally recognized as safe (GRAS) for use as (1) a pH control agent and leavening agent in cake mixes at a level of 1 to 10 grams sodium bisulfate per 1000 grams of total mix (0.1 per cent to 1.0 per cent by weight) and (2) a pH control agent and a processing aid in food at levels not to exceed good manufacturing practice. Your notice refers to the provision in 21 CFR 184.1095 (sulfuric acid) that current good manufacturing practice results in a maximum level, as served, of 0.014 per cent for alcoholic beverages and 0.0003 per cent for cheeses. Your notice describes the manufacturing process for sodium bisulfate, which is the sodium salt of sulfuric acid. The manufactured sodium bisulfate meets the specifications for this ingredient in the Food Chemicals Codex, Fourth Edition (1996). Its main characteristic is its acidity in water solutions.

Your notice states that the basis for the GRAS determination is through experience based on common use in food - i.e., that Jones-Hamilton Co. has experience based on common use in food. However, as we discussed by telephone on April 27, 1998, FDA considered your notice under scientific procedures (§ 170.30(b)). Based on the information provided by Jones-Hamilton Co., as well as other information available to FDA, the agency has no questions at this time regarding the conclusion of Jones-Hamilton Co. that sodium bisulfate is GRAS under the proposed conditions of use. The agency has not, however, made its own determination regarding the GRAS status of the subject use of sodium bisulfate. As always, it is your continuing

responsibility to ensure that food ingredients that you market are safe, and are otherwise in compliance with all applicable legal and regulatory requirements.

In accordance with proposed 21 CFR 170.36(f), a copy of this letter has been made available for public review and copying at the agency's Dockets Management Branch (Docket No. 98S-0104). As mentioned in our letter dated March 5, 1998, which acknowledged receipt of your GRAS notice, a copy of the information in your notice that conforms to the information in proposed § 170.36(c)(1) is likewise available in Docket No. 98S-0103.

Sincerely,

Alan M. Rulis, Ph.D.
Director
Office of Premarket Approval
Center for Food Safety and Applied Nutrition

-
http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/GRASListings/ucm154921.htm

Appendix IV: WHO Food Additive Series #44 (2000).

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

WORLD HEALTH ORGANIZATION

SAFETY EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS

WHO FOOD ADDITIVES SERIES: 44

Prepared by the Fifty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA)

World Health Organization, Geneva, 2000
IPCS - International Programme on Chemical Safety

SODIUM SULFATE

First draft prepared by Dr J.B. Greig

Joint Food Safety & Standards Group, Department of Health, London, United Kingdom

1. EXPLANATION

Sodium sulfate has not been evaluated previously by the Committee. The sulfate anion was evaluated at the twenty-ninth meeting (Annex 1, reference 70), when an ADI 'not specified' was established, since sulfate is a natural constituent of food and is a product of sulfur metabolism in animals. Sodium sulfate was not specifically included in that ADI because no information was available to indicate that it was being manufactured or used as a food-grade material. It was evaluated at the present meeting at the request of the Codex Committee on Food Additives and Contaminants because it is being considered for inclusion in the draft General Standard for Food Additives.

The Committee were unaware of any data on the dietary intake of sodium sulfate in human populations.

2. BIOLOGICAL DATA

2.1 Renal clearance of the sulfate anion

The renal clearance of the sulfate ion was measured in a cross-over clinical trial in six men and two women, aged 26-35, weighing 45-98 kg, and with an estimated body surface area of 1.4-2.2 m^2. On different, randomized study days at least four days apart, 1-2 h after a light breakfast (hour 0), the subjects drank either 100 ml water or a solution of 4.5 g sodium sulfate decahydrate in 100 ml water. This dose was repeated at hour 1, at which time the subjects emptied their bladders. Urine was then collected from hour 1 to hour 3, and a blood sample was taken at hour 2.

The serum concentration of sulfate at hour 2 and the 2-h urinary excretion of sulfate anion were both statistically significantly increased after the sulfate dose: mean ± SD, 0.51 ± 0.05 vs 0.41 ± 0.04 mmol/L and 2.4 ± 0.87 vs 1.6 ± 0.46 mmol/L × 73 m^2 body surface area. The renal clearance of sulfate after the sulfate dose was greater than that after water, but the difference was not statistically significant. The authors also reported, with no details, that in a separate experiment, a 6-g oral dose of ascorbic acid had no effect on the urinary excretion of endogenous inorganic sulfate over 12 h (Morris & Levy, 1983).

In another randomized, cross-over clinical trial from the same laboratory, eight healthy men aged 23-26 and weighing 70-100 kg received 4.5 g of sodium sulfate as the decahydrate in water at 0, 2, 4, and 6 h and 10 g activated charcoal suspended in water at hour 0, separately or in combination, after treatment with acetaminophen. When sodium sulfate was included in the treatment, the mean quantity of acetaminophen sulfate excreted in the urine increased but the difference from the treatment without sodium sulfate did not achieve statistical significance. The increase in the 24-h urinary excretion of sulfate anion was statistically significant, whether activated charcoal was included in the treatment or not (Galinsky & Levy, 1984).

2.2 Toxicological studies

2.2.1 Long-term studies

Mice

In a poorly reported study, 50 male and 50 female Swiss albino mice aged six weeks received 4-(hydroxymethyl)benzenediazonium sulfate by subcutaneous injection weekly for 26 weeks with 31 µg of sodium sulfate dissolved in 0.01 ml of 0.9% saline. The mice were then kept for life. Tumours of the skin and subcutis were described as occurring at incidences similar to those of untreated laboratory historical controls; however, although tumours also developed in other tissues no similar statement was made (Toth, 1987).

2.2.2 Developmental toxicity

Mice

As part of a study of the teratogenicity of morphine sulfate and other pharmacological agents, groups of pregnant CF-1 albino mice were injected subcutaneously on gestation day 8 or 9 with sodium sulfate at 60 mg/kg bw given as 10 mg/ml in water. Examination of the excised fetuses revealed some statistically significant differences from saline-treated controls, but none of the measured parameters was consistently affected. Although skeletal abnormalities were observed in both groups, the difference seen from saline controls after dosing on day 9 of gestation was not significant, and the anomalies did not appear to involve fusions of the axial skeleton (Arcuri & Gautieri, 1973).

Sodium sulfate was included in a test of a method for rapid assessment of teratogenicity. Pregnant ICR/SIM mice were given a saturated aqueous solution of sodium sulfate orally by gavage to deliver a dose of 2800 mg/kg bw per day on days 8-12 of gestation. No maternal deaths occurred and the average maternal weight gain during the treatment period was not significantly different from that of water-treated controls. Twenty-four litters were delivered alive, and none were resorbed. The mean numbers of neonates delivered alive and dead in each litter and the survival of neonates on day 3 were not statistically significantly different from those of controls. Neonatal body weights on days 1 and 3 and body-weight gain were recorded; only body weight on day 1 was statistically significantly greater than that of controls (Seidenberg et al., 1986).

2.3 Observations in humans

2.3.1 General observations

Sodium sulfate decahydrate is listed in the *British Pharmacopoeia* as having the action and use of a laxative, and it is recorded as complying with the requirements of the third edition of the *European Pharmacopoeia* (Department of Health, 1993, 1996). Sodium sulfate decahydrate and its anhydrous salt are listed in *Martindale's Pharmacopoeia*, and the laxative use is noted; another medical use recorded is in the treatment of severe hypercalcaemia, in which it is given by slow intravenous administration of a 3.9% aqueous solution. It is also used as a diluent for food colours (Reynolds, 1996).

2.3.2 Occupational exposure

A group of 119 workers in five sodium sulfate surface mines in Saskatchewan, Canada (selection criteria and response rate not stated) were studied. There was no control group. The workers were aged 17-58 years, and since the values for lung function were compared with those reported for men, it can be assumed that they were male. The concentrations of sodium sulfate dust in various work areas were reported to be 5, 40, and 150 mg/m^3, but although some consideration was given to the extent and duration of exposure there was no stratification by integrated measures of exposure × time. Worker were classified as having had more (n = 42) or less (n = 77) than 10 years of exposure. The workers were screened for lung disease,

hypertension, oedema, calcium tetany, anaemia, dermatitis, perforation of the nasal septum, and frequent or persistent diarrhoea. Serum was analysed for calcium, sodium, and potassium cations, chloride and sulfate anions, and carbon dioxide. Urine was analysed for sulfate content.

The physical parameters measured, including serum sulfate, calcium, and serum electrolytes, were generally within the normal range of values. Erythema or hyperaemia of the nasal mucosa was seen in 24 subjects, and exposure to sodium sulfate dust was associated with nasal irritation followed by a runny nose. No obvious association with extent of exposure was seen for six workers who had below-normal values for lung function, and some of these workers were heavy smokers. There was no statistically significant difference between workers with more and those with less than 10 years of exposure with respect to lung function. The serum sulfate concentration of one worker was above the normal range. Urinary excretion of sulfate was 0.90-4.9 g/L, and 30% of the workers excreted more than 3 g/L. Since there was no association with duration of exposure, the authors suggested that these high values could be attributed to recent exposure (Kelada & Euinton, 1978).

2.3.3 Use of purgative preparations

2.3.3.1 Clinical trials

A prospective study was carried out on the basis of responses to a questionnaire about use at home of two bowel-cleansing preparations, sodium picosulfate and a polyethylene glycol preparation containing 40 mmol/L of sodium sulfate. At follow-up after three months to detect any serious adverse effects, 165 patients (94% male) were recruited into the study, 82 of whom (mean age, 60 years; range, 22-86) had taken the polyethylene glycol preparation. Of these, eight had failed to take the full 4 L, 12 reported faecal incontinence, and 21 reported sleep disturbances. A statistically significant greater number of complaints from younger patients about taste disturbance, nausea, fullness, and cramp was not attributed specifically to either preparation (Heymann et al., 1996).

In the study of the renal clearance of sodium sulfate described in section 2.1.1, administration of two doses of 4.5 g sodium sulfate decahydrate in 100 ml water at an interval of 1 h had no adverse effects except for occasional loose stools (Morris & Levy, 1983). Similarly, in another study from the same laboratory, only a few instances of loose stools were reported by persons who took four doses of an aqueous solution of 4.5 g sodium sulfate decahydrate (Galinsky & Levy, 1984).

2.3.3.2 Case reports

A 39-year-old woman who had attempted suicide by taking 40 g of barium carbonate was treated after gastric lavage with 60 g of sodium sulfate administered through a nasogastric tube and 2.5 g of magnesium sulfate intravenously. The subsequent development of progressive renal insufficiency was suggested to have been caused by precipitation of barium sulfate in the renal tubules (Phelan et al., 1984).

A 45-year old woman with a history of coronary heart disease, thoracic aortic aneurysm, and multiple myocardial infarcts experienced exacerbation of her congestive heart failure after ingestion of a bowel preparation containing 240 g polyethylene glycol 3350, 23 g sodium sulfate, 6.7 g sodium bicarbonate, 5.9 g sodium chloride, and 3 g potassium chloride reconstituted in 4 L of water and drunk at a rate of 240 ml every 10 min (Granberry et al., 1995).

An 8.5-year-old girl with cystic fibrosis and associated disturbance of liver function became drowsy and had a hypoglycaemic convulsion after she ingested 1.2 L of a bowel-cleansing preparation based on polyethylene glycol 4000 and containing 40 mmol/L sodium sulfate over a period of 1 h (Shah et al., 1994).

3. COMMENTS

The Committee considered that the results of the published studies in experimental animals do not raise concern about the toxicity of sodium sulfate. The compound has a laxative action, which is the basis for its clinical use. The minor adverse effects reported after use of ingested purgative preparations containing sodium sulfate may not be due to the sodium sulfate itself.

4. EVALUATION

In the absence of any evidence of toxicity, the Committee allocated a temporary ADI 'not specified'[1] in line with the principles established at its twenty-ninth meeting. The ADI was made temporary because no information was available on the functional effect and actual uses of sodium sulfate in foods. This information is required for evaluation in 2001.

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[1] ADI 'not specified' is a term applicable to a food component of very low toxicity which, on the basis of the available chemical, biological, toxicological, and other data, the total dietary intake of the substance arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food, does not, in the opinion of the Committee, represent a hazard to health. For this reason and for those stated in the evaluation, the establishment of an ADI expressed in numerical form is deemed unnecessary.

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See Also:
Toxicological Abbreviations
Sodium sulfate (ICSC)
SODIUM SULFATE (JECFA Evaluation)
Sodium sulfate (SIDS)

Appendix V: WHO Food Additive Series # 62 2010a

WHO FOOD ADDITIVES SERIES: 62

Safety evaluation of certain food additives

Prepared by the
Seventy-first meeting of the Joint FAO/WHO
Expert Committee on Food Additives (JECFA)

Food and Agriculture Organization of the United Nations

World Health Organization

WHO FOOD ADDITIVES SERIES: 62

Safety evaluation of certain food additives

Prepared by the
Seventy-first meeting of the Joint FAO/WHO
Expert Committee on Food Additives (JECFA)

World Health Organization, Geneva, 2010

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(WHO food additives series ; 62)

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CONTENTS

PREFACE

The monographs contained in this volume were prepared at the seventy-first meeting of the Joint Food and Agriculture Organization of the United Nations (FAO)/ World Health Organization (WHO) Expert Committee on Food Additives (JECFA), which met at WHO headquarters in Geneva, Switzerland, on 16–24 June 2009. These monographs summarize the data on selected food additives reviewed by the Committee.

The seventy-first report of JECFA has been published by the World Health Organization as WHO Technical Report No. 950. Reports and other documents resulting from previous meetings of JECFA are listed in Annex 1. The participants in the meeting are listed in Annex 3 of the present publication.

JECFA serves as a scientific advisory body to FAO, WHO, their Member States and the Codex Alimentarius Commission, primarily through the Codex Committee on Food Additives, the Codex Committee on Contaminants in Food and the Codex Committee on Residues of Veterinary Drugs in Foods, regarding the safety of food additives, residues of veterinary drugs, naturally occurring toxicants and contaminants in food. Committees accomplish this task by preparing reports of their meetings and publishing specifications or residue monographs and toxicological monographs, such as those contained in this volume, on substances that they have considered.

The monographs contained in this volume are based on working papers that were prepared by temporary advisers. A special acknowledgement is given at the beginning of each monograph to those who prepared these working papers. The monographs were edited by M. Sheffer, Ottawa, Canada.

Many unpublished proprietary reports are unreferenced. These were voluntarily submitted to the Committee by various producers of the food additives under review and in many cases represent the only data available on those substances. The temporary advisers based the working papers they wrote on all the data that were submitted, and all these reports were available to the Committee when it made its evaluations.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the organizations participating in WHO concerning the legal status of any country, territory, city or area or its authorities, or concerning the delimitation of its frontiers or boundaries. The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the organizations in preference to others of a similar nature that are not mentioned.

Any comments or new information on the biological or toxicological properties of the compounds evaluated in this publication should be addressed to: Joint WHO Secretary of the Joint FAO/WHO Expert Committee on Food Additives, Department of Food Safety and Zoonoses, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

SODIUM HYDROGEN SULFATE

First draft prepared by

Ms R.A. Harrison,[1] Dr D.J. Benford,[1] Professor R. Walker[2] and Ms J. Baines[3]

[1] Food Standards Agency, London, England
[2] University of Surrey, Guildford, Surrey, England
[3] Food Standards Australia New Zealand, Canberra, Australian Capital Territory, Australia

1. EXPLANATION

At the present meeting, the Committee evaluated sodium hydrogen sulfate for use as an acidifier, at the request of the Codex Committee on Food Additives at its fortieth session (FAO/WHO, 2008). The Committee was asked for a safety assessment and revision of specifications. At its sixty-eighth meeting, the Committee considered sodium hydrogen sulfate for use in the preparation of acidified sodium chlorite, an antimicrobial washing solution, and established specifications, but did not evaluate it for safety (Annex 1, reference *187*). At its ninth and twenty-third meetings, the Committee evaluated a large number of food acids and salts and was of the opinion that acceptable daily intakes (ADIs) for ionizable salts should be based on previously accepted recommendations for the constituent cations and anions (Annex 1, references *11* and *50*).

The sulfate ion was evaluated at the twenty-ninth meeting of the Committee (Annex 1, reference *70*), when an ADI "not specified" was established, as sulfate is a natural constituent of food and is a product of sulfur metabolism in animals. Sodium sulfate was evaluated at the fifty-third, fifty-fifth and fifty-seventh meetings

(Annex 1, references *144*, *149* and *154*), when an ADI "not specified" was established.

The Committee decided to assess sodium hydrogen sulfate in terms of the sulfate component because of its dissociation to the constituent ions and given that sodium and hydrogen ions are ubiquitous and natural constituents of foods.

1.1 Chemical and technical considerations

Sodium hydrogen sulfate is manufactured by mixing sodium chloride with sulfuric acid at elevated temperatures to form molten sodium hydrogen sulfate. The molten sodium hydrogen sulfate is sprayed and cooled to form a solid product with uniform particle size.

2. BIOLOGICAL DATA

2.1 Biochemical aspects

Renal clearance data for the sulfate anion were included in the Committee's evaluation of sodium sulfate at its fifty-third meeting (Annex 1, reference *144*). No additional information was located.

2.2 Toxicological studies

2.2.1 Studies on sodium hydrogen sulfate

Groups of male and female Sprague-Dawley rats were gavaged with sodium hydrogen sulfate at a single oral dose of 1750, 2000, 2250, 2500, 3000 or 3500 mg/kg body weight (bw) to determine its acute oral toxicity. Fifty-five animals were treated in total. Control rats were similarly dosed with deionized water. Surviving animals were killed after 14 days. The oral median lethal dose (LD_{50}) was determined to be 2800 mg/kg bw in males and >2500 mg/kg bw in females. Fewer females than males died. As the test progressed, it was decided to stop dosing the females, as it was clear that the LD_{50} was above 2500 mg/kg bw. Effects observed during the study included weight loss, dehydration, scruffy coats, lethargy and death. Gross abnormalities observed in the animals that died during the study included mottled red lungs, pale mottled livers and stomach lesions or ruptures (Northview Pacific Laboratories, 1990).

2.2.2 Studies on sulfate

Artificially reared neonatal piglets were used as a model to evaluate the effect of inorganic sulfate on bowel function in human infants. Two experiments were conducted. The first evaluated the effect of high levels of sulfate on growth, feed intake and consistency of faeces, and the second determined the dose at which at least 50% of the pigs developed non-pathogenic diarrhoea. Following a 5-day acclimatization period, 40 piglets were distributed into four groups for each experiment. Piglets were fed liquid diets only via an Autosow and did not have access to drinking-water. Inorganic sulfate was added to the diets as anhydrous

sodium sulfate at levels of 0, 1200, 1600 and 2000 mg/l for experiment 1 (18-day study) and 0, 1800, 2000 and 2200 mg/l for experiment 2 (16-day study). Piglets were individually caged and weighed daily, and the volume of diet for each piglet was adjusted according to its body weight. Feed intake and consistency of faeces were recorded 3 times daily. Rectal swabs were taken from those piglets with soft or liquid stools and analysed for haemolytic *Escherichia coli* and rotavirus. At the end of each experiment, piglets were sedated and killed. Urine samples were taken, and the kidneys were removed. The levels of added sulfate did not affect the growth of the piglets or their feed intake. Levels of 2000 and 2200 mg sulfate/l resulted in practically all (90–100%) piglets having diarrhoea, beginning 2 days after the start of the trial and persisting throughout the experimental period. Rectal swabs were negative, from which the authors concluded that the piglets had non-pathogenic diarrhoea. Kidney weight was not affected by added sulfate. Sulfate concentrations in the urine reached a maximum in the piglets fed diets with 1600 and 1800 mg sulfate/l in experiments 1 and 2, respectively ($P < 0.05$), but declined at higher levels. Based on the results, the authors concluded that the concentration of added sulfate at which 50% of piglets develop non-pathogenic diarrhoea is between 1600 and 1800 mg/l (Gomez et al., 1995).

2.3 Observations in humans

In 1999, the United States Environmental Protection Agency and Centers for Disease Control and Prevention conducted a study on the health effects from exposure to high levels of sulfate in the drinking-water in two sensitive populations (infants and transient adults). For the infant study, the authors intended to conduct a prospective cohort study of newborn infants whose mothers planned to feed their infants formula mixed with tap water. However, a pilot study involving a self-administered questionnaire to all women attending 32 clinics to determine how many women planned to use tap water to mix infant formula for their babies revealed that very few infants were exposed to tap water containing high levels of sulfate.

One hundred and five adult volunteers were randomly assigned to one of five sulfate groups: 0 mg/l ($n = 24$), 250 mg/l ($n = 10$), 500 mg/l ($n = 10$), 800 mg/l ($n = 33$) or 1200 mg/l ($n = 28$). Bottled water was provided for the volunteers for 6 days. The bottled water for days 1, 2 and 6 was unsupplemented, whereas the bottles for days 3–5 contained water with added sulfate. Bottles were returned to estimate how much water was consumed each day. Volunteers recorded the number of bowel movements each day. There were no statistically significant differences in the bowel movements among the groups on days 3–6, nor were there any statistically significant differences in the bowel movements when comparing days 1 and 2 with days 3–5, within each dose group. The authors concluded that there was no statistically significant increase in reports of diarrhoea with increasing dose of sulfate in the drinking-water (United States Environmental Protection Agency, 1999).

3. DIETARY EXPOSURE

Sodium hydrogen sulfate is an acid and can be added to foods to lower pH, to improve shelf life and/or improve flavour. Typically, sodium hydrogen sulfate may be added to beverages, confectionery, fillings, syrups, salad dressings and sauces. It is stronger than organic acids such as citric acid, so lower amounts are required to reach the same pH. Because it does not impart a sour or citric taste, as do other acidifiers, it can be used in products where these are not desirable—for example, in non-citrus-flavoured soft drinks, tea, chocolate-flavoured drinks and coffee-flavoured drinks (personal communication from C. Kneuven, Jones-Hamilton Co., to WHO, 2008).

Typical use levels for a variety of food categories and poundage data were given by the food industry (personal communication from C. Kneuven, Jones-Hamilton Co., to WHO, 2008). Although most uses were at 2000 mg/kg or less, the highest use level reported was 4000 mg/kg for processed cheeses, soup and soup mixes (Table 1).

Table 1. Typical use levels for sodium hydrogen sulfate

Food category	Typical use level	
	mg/kg	%
Beverages	600	0.06
Confectionery, fillings and syrups	1000	0.1
Processed cheeses	4000	0.4
Dressings and sauces	2000	0.2
Jams and jellies	800	0.08
Processed vegetables and vegetable juices	3000	0.3
Soups and soup mixes	4000	0.4
Salsa	500	0.05

3.1 Screening by the budget method

As no ADI has been allocated to sodium hydrogen sulfate and as sodium sulfate has an ADI "not specified", it was not possible to undertake a budget method calculation.

3.2 Poundage data

The annual poundage of sodium hydrogen sulfate sold into the North American and European markets was reported in the food industry submission to be approximately 2000 tonnes, with 1900 tonnes being used in North America and 100 tonnes in Europe (personal communication from C. Kneuven, Jones-Hamilton Co., to WHO, 2008). It was noted that production volumes could potentially increase to a total of 5000 tonnes in the future.

Per capita dietary exposures can be calculated by applying a correction factor of 0.8 for under-reporting of the amount of additive produced. In this case, it was assumed that all consumers may be exposed to the additive, as non-alcoholic beverages, confectionery, sauces, soups and cheese products are widely consumed. Per capita dietary exposure to sodium hydrogen sulfate for the USA was estimated to be between 22 and 54 mg/day and for Europe between 0.4 and 1 mg/day (USA population 30×10^7 in 2006, European population 80×10^7 in 2008), for current and projected production volumes, respectively, assuming the same proportion of use between the USA and Europe.

3.3 Dietary exposure based on national nutrition surveys

Potential dietary exposures to sodium hydrogen sulfate were estimated for several European countries using information on diets from the European Food Safety Authority's Concise European Food Consumption Database (European Food Safety Authority, 2009), derived from national nutrition surveys. Potential mean dietary exposures and high-consumer exposures to sodium hydrogen sulfate were calculated for the whole adult population aged 16–64 years for the 19 countries in the database, assuming that sodium hydrogen sulfate was used at typical use levels in broad food categories where use is proposed. High-consumer dietary exposures were estimated by taking consumption for two food categories with the highest dietary exposure at the 95th percentile plus mean exposures for the whole population for all other food categories (European Food Safety Authority, 2008). Potential mean dietary exposures for the whole adult population for each country ranged from 400 to 1160 mg/day; for high consumers of sodium hydrogen sulfate, potential dietary exposures ranged from 1090 to 6340 mg/day (Table 2). Major contributors to total dietary exposure were fruit and vegetable juices, vegetable soups, non-alcoholic beverages with a low percentage of fruit, tea and coffee, and cheese.

Table 2. Potential dietary exposure to sodium hydrogen sulfate for adults in 19 European countries (based on food consumption data sourced from the Concise European Food Consumption Database)[a]

Country	Survey	Model	Dietary exposure (mg/day)
Austria	2005–2006 Austrian Study on Nutritional Status 19–64 years; 24-h recall (2123 respondents)	Mean all	1010
		High consumer	5530
Belgium	2004 Belgian Food Consumption Survey 16–64 years, 24-h recall over 2 days (1723 respondents)	Mean all	1130
		High consumer	4190

Table 2. (contd)

Country	Survey	Model	Dietary exposure (mg/day)
Bulgaria	2004 National Survey of Food Intake and Nutritional Status 16–64 years, 24-h recall (853 respondents)	Mean all	460
		High consumer	2910
Czech Republic	2003–2004 Individual Food Consumption Study 16–64 years, 24-h recall (1751 respondents)	Mean all	690
		High consumer	2600
Denmark	200–2002 Danish National Dietary Survey (DK2002) 4–65 years, diary over 7 days (4439 respondents)	Mean all	1000
		High consumer	2550
Estonia	1997 Estonian Adult Nutrition Survey 16–64 years, 24-h recall (2018 respondents)	Mean all	420
		High consumer	1090
Finland	2002 National Findiet Study 25–64 years, 24-h recall over 2 days (2007 respondents)	Mean all	520
		High consumer	1280
France	1999 Enquête Individuelle et Nationale sur les Consommations Alimentaires (INCA) 15+ years over 7 days (1474 respondents)	Mean all	820
		High consumer	2660
Germany	1998 German Nutrition Survey 18+ years, diet history over 28 days (4030 respondents)	Mean all	1160
		High consumer	3140
Hungary	2003–2004 Hungarian National Dietary Survey 18+ years, dietary record over 3 days (1179 respondents)	Mean all	440
		High consumer	1600
Iceland	2002 The Diet of Icelanders 15–80 years, 24-h recall (1075 respondents)	Mean all	990
		High consumer	4990

Table 2. (contd)

Country	Survey	Model	Dietary exposure (mg/day)
Ireland	1997–1998 North/South Ireland Food Consumption Survey (NSIFCS) 15–80 years, dietary record over 7 days (1369 respondents)	Mean all	760
		High consumer	1630
Italy	1994–1996 Nationwide Nutritional Survey of Food Behaviour (INN-CA) 16–64 years, dietary record over 7 days (1544 respondents)	Mean all	400
		High consumer	1090
The Netherlands	1997–1998 Dutch National Food Consumption Survey All ages, dietary record over 2 days (6250 respondents)	Mean all	1080
		High consumer	3040
Norway	1993–1997 Norwegian National Dietary Survey 16+ years, food frequency survey (2352 respondents)	Mean all	1030
		High consumer	2240
Poland	2000 Household Food Consumption and Anthropometric Survey (HFCAAS) 1–96 years, 24-h recall (4134 respondents)	Mean all	770
		High consumer	3560
Slovakia	2006 Monitoring of Nutritional Status of Adult Population 19–54 years, 24-h recall (2208 respondents)	Mean all	1160
		High consumer	6340
Sweden	1997–1998 Dietary Habits and Nutrient Intake in Sweden 17+ years, dietary record over 7 days (1210 respondents)	Mean all	860
		High consumer	2240

Table 2. (contd)

Country	Survey	Model	Dietary exposure (mg/day)
United Kingdom	2000–2001 National Diet and Nutrition Survey (NDNS) 19–64 years over 7 days (1724 respondents)	Mean all	930
		High consumer	2220

[a] Assumptions for all countries:

1. Summary statistics for 16- to 64-year age group only, where data available.
2. Typical use levels for food categories applied to broad food group: "Sugar & sugar products including chocolate" at 1000 mg/kg, "Vegetable soups" at 4000 mg/kg, "Fruit & vegetable juice" at 3000 mg/kg, "Soft drinks" at 600 mg/kg, "Coffee, tea, cocoa" at 600 mg/kg, "Cheese" at 4000 mg/kg, "Miscellaneous foods including foods for special dietary uses" at 2000 mg/kg.
3. High-consumer estimate derived from consumption for two food groups with highest dietary exposure at the 95th percentile plus mean for population for all other food groups.

It should be noted that basing potential dietary exposures on the amounts of food consumed for 15 broad food categories given in the European diets will overestimate the dietary exposure to sodium hydrogen sulfate. The actual use of sodium hydrogen sulfate would be restricted to subgroup categories within the broader food group and to foods within these subgroups where a low pH is required and an acidic or citric taste is undesirable. For example, in these estimates, the typical use level for processed cheese was assigned to all cheeses, thus overestimating the potential contribution from cheese; the typical use level for beverages was assigned to all tea and coffee, thus overestimating the potential contribution from these beverages, as in reality the food additive would be used only in some flavoured teas and coffees. In addition, for the European Food Safety Authority food group 2, "sugar and sugar-containing products", the higher of two concentrations given for products within this category was used (2000 mg/kg for confectionery, fillings and syrups), which would overestimate the contribution from the "jams and jellies" subcategory, where typical use was reported at 800 mg/kg.

A more accurate dietary exposure estimate for the Australian population was also determined, based on individual dietary records and typical levels of use for specific food groups within broader food categories, as notified in the food industry submission (Table 3). For example, the typical use level for beverages was assigned to flavoured teas, soft drinks, fruit and vegetable juices, fruit drinks and dry beverage preparations, rather than to all non-alcoholic beverages. Potential mean dietary exposures for the whole population were 700 mg/day. For consumers of foods containing sodium hydrogen sulfate only, potential mean dietary exposures of 740 mg/day were similar to those for the whole population, as the additive can be used in a wide range of foods; dietary exposures for high consumers at the 90th percentile were 1210 mg/day. The major contributors to total potential dietary exposure were soups and soup mixes (45%), water-based flavoured drinks (22%) and fruit and vegetable preparations (15%).

Table 3. Potential dietary exposure to sodium hydrogen sulfate for the Australian population (based on individual dietary records)

Survey	Assumptions	Model	Dietary exposure	
			mg/day	mg/kg bw per day[a]
1995 National Nutrition Survey aged 2+ years 24-h recall (13 858 respondents, of whom 94% were consumers)	Typical levels of use for all listed food categories (Table 1)	Mean all	700	11.8
		Mean consumers	740	12.8
		90th-percentile consumers	1210	21.9

[a] Individual body weights were used in the calculations (mean body weight for the Australian population was 67 kg).

4. COMMENTS

4.1 Toxicological data

When sodium hydrogen sulfate is added to food products containing water or after ingestion of sodium hydrogen sulfate, it ionizes to sodium ions, hydrogen ions and sulfate ions. The Committee received a submission containing unpublished studies on sodium hydrogen sulfate, including a study on its acute toxicity and studies on inhalation toxicity, skin irritation and corrosivity, and freshwater ecotoxicity. A literature search identified no published studies of the toxicity of sodium hydrogen sulfate. Additional information identified by a literature search related to sulfate, as the Committee decided to assess sodium hydrogen sulfate in terms of the sulfate component because of its dissociation to the constituent ions and given that sodium and hydrogen ions are ubiquitous and natural constituents of foods.

In an acute toxicity study, the oral LD_{50} of sodium hydrogen sulfate in rats was determined to be 2800 mg/kg bw in males and >2500 mg/kg bw in females. The additional studies received as part of the submission were not considered relevant to the evaluation of the oral toxicity of sodium hydrogen sulfate.

In studies evaluating the effect of inorganic sulfate on bowel function, the body weight and kidney weight of neonatal pigs administered up to 2000 mg/l in a liquid diet for 18 days were unaffected. In a 16-day study, the concentration of added sulfate in the diet at which 50% of the piglets developed non-pathogenic diarrhoea was estimated to be between 1600 and 1800 mg/l. No differences in bowel movements were noted in adult volunteers receiving sulfate in the drinking-water at concentrations up to 1200 mg/l for 3 consecutive days.

The additional studies identified on sulfate did not raise concern about its toxicity.

4.2 Assessment of dietary exposure

Sodium hydrogen sulfate is typically added to beverages, confectionery, fillings, syrups, processed cheeses, salad dressings, sauces, jams and jellies, and processed vegetable products at levels ranging from 500 to 4000 mg/kg. For beverages, sodium hydrogen sulfate is generally used in non-citrus-flavoured soft drinks, tea, and chocolate-flavoured and coffee-flavoured drinks, as it does not impart a sour or citric taste, as do other acidifiers.

Based on poundage data for the USA, where the food additive has the highest reported production levels, mean per capita exposures for the population in the USA for current production volumes and for increased production volumes in the future, as predicted by the sponsor, were estimated to be 20 and 50 mg/day, respectively, assuming that all members of the population were consumers of products containing the additive.

From the limited data submitted by the sponsor on the proposed use of sodium hydrogen sulfate as a food acid, potential mean and high-consumer dietary exposures (derived from consumption for two food groups with highest dietary exposure at the 95th percentile plus mean for population for all other food groups) for 19 European populations (aged 16–64 years) were calculated based on typical use levels, assuming that the additive was used in all foods in each of the broad food categories identified above. Potential mean per capita dietary exposures for this "worst case" scenario ranged from 400 to 1160 mg/day for the whole population and from 1090 to 6340 mg/day for high consumers of foods containing sodium hydrogen sulfate. Potential dietary exposures based on individual dietary records and use of sodium hydrogen sulfate in food subcategories specified by the sponsor were submitted for the Australian population. Potential mean dietary exposures for Australians were lower than those for Europeans but of the same order of magnitude (mean per capita dietary exposure of 700 mg/day for the whole Australian population and 1210 mg/day for high consumers at the 90th percentile). The Committee considered that the predicted dietary exposures for the European and Australian populations were overestimates, a view supported by the much lower per capita estimates reported for the population in the USA. The actual use of sodium hydrogen sulfate would be restricted to subcategories within the broader food group and to foods within these subcategories where a low pH was required and/or for drinks where an acidic or citric taste was undesirable.

5. EVALUATION

Considering that the available evidence did not provide any indication of toxicity, the Committee allocated an ADI "not specified" for sodium hydrogen sulfate, in line with the principles established for ionizable salts at its twenty-ninth meeting, when used in the applications specified and in accordance with Good Manufacturing Practice.

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ANNEXES

ANNEX 1

REPORTS AND OTHER DOCUMENTS RESULTING FROM PREVIOUS MEETINGS OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

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13. *Specifications for the identity and purity of food additives and their toxicological evaluation: some emulsifiers and stabilizers and certain other substances* (Tenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 43, 1967; WHO Technical Report Series, No. 373, 1967.
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ANNEX 2

ABBREVIATIONS USED IN THE MONOGRAPHS

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism and elimination
ALT	alanine aminotransferase
AP	alkaline phosphatase
AST	aspartate aminotransferase
BEU	branching enzyme units
BROD	benzyloxyresorufin *O*-dealkylase
bw	body weight
CCFA	Codex Committee on Food Additives
CSFII	Continuing Survey of Food Intakes by Individuals (USA)
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
EC_{50}	median effective concentration
EDTA	ethylenediaminetetraacetate
EFSA	European Food Safety Authority
EROD	ethoxyresorufin *O*-deethylase
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
GEGR	glycerol ester of gum rosin
GEWR	glycerol ester of wood rosin
GLP	Good Laboratory Practice
GR	gum rosin
GRAS	Generally Recognized as Safe
GSFA	General Standard for Food Additives (Codex)
GST	glutathione transferase
HDL	high-density lipoprotein
HEPES	*N*-2-hydroxyethylpiperazine-*N*'-2-ethanesulfonic acid
HPLC	high-performance liquid chromatography
IQ	intelligence quotient
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD_{50}	median lethal dose
LDL	low-density lipoprotein
LOAEL	lowest-observed-adverse-effect level
LSC	liquid scintillation counting
MROD	methoxyresorufin *O*-demethylase
NCE	normal chromatic erythrocyte
NDMAD	*N*-nitrosodimethylamine *N*-demethylase
NHANES	National Health and Nutrition Examination Survey (USA)
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
OECD	Organisation for Economic Co-operation and Development

OSA	octenyl succinic acid
PCE	polychromatic erythrocyte
PhIP	2-amino-1-methyl-6-phenylimidazo [4,5-*b*]pyridine
PROD	pentoxyresorufin *O*-dealkylase
QA	quality assurance
QR	quinone reductase
S9	9000 × *g* supernatant from rat liver
SCF	Scientific Committee on Food (European Commission)
SOE	sucrose oligoesters
TOR	tall oil rosin
TOS	total organic solids
TPPO	triphenyl phosphine oxide
U	uniformly
UDP	uridine 5′-diphosphate
UDPGT	uridine 5′-diphosphate glucuronosyltransferase
USA	United States of America
USFDA	United States Food and Drug Administration
UV	ultraviolet
WHO	World Health Organization
WR	wood rosin

ANNEX 3

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

Geneva, 16–24 June 2009

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ANNEX 4

ACCEPTABLE DAILY INTAKES, OTHER TOXICOLOGICAL INFORMATION AND INFORMATION ON SPECIFICATIONS

1. FOOD ADDITIVES EVALUATED

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
Branching glycosyltransferase from *Rhodothermus obamensis* expressed in *Bacillus subtilis*	N	The Committee allocated an ADI "not specified" for branching glycosyltransferase from *Rhodothermus obamensis* expressed in *Bacillus subtilis* used in the specified applications and in accordance with Good Manufacturing Practice.
Cassia gum	N, T	The Committee allocated an ADI "not specified" for cassia gum that complies with the tentative specifications established at the current meeting, when used in the applications specified and in accordance with Good Manufacturing Practice. The Committee decided to make the specifications tentative pending submission of data on a suitable and validated method for determination of anthraquinones at a level of 0.5 mg/kg and below, by the end of 2010.
Cyclamic acid and its salts (dietary exposure assessment)		Of the four maximum use levels (250, 500, 750 and 1000 mg/kg) that the Committee considered at the request of the Codex Committee on Food Additives (CCFA) for cyclamates in beverages covered by General Standard for Food Additives (GSFA) Food Category 14.1.4, only the lowest level of 250 mg/kg was not likely to lead to dietary exposures exceeding the ADI for high consumers, including children. Moreover, it was noted that a maximum use level of 350 mg/kg also resulted in dietary exposures for high consumers, including children, that were less than the ADI.
Cyclotetraglucose and cyclotetraglucose syrup	R (cyclotetraglucose syrup)	The Committee removed the temporary designation and established an ADI "not specified" for cyclotetraglucose and cyclotetraglucose syrup. The specifications for cyclotetraglucose syrup were revised, and the tentative designation was removed.
Ferrous ammonium phosphate	N	The newly available information on the toxicity of iron did not indicate a need to revise the

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
		provisional maximum tolerable daily intake (PMTDI) of 0.8 mg/kg body weight (bw). Consideration of the toxicity of ammonium and phosphate did not indicate a need to revise the Committee's previous evaluations of these ions. The Committee concluded that ferrous ammonium phosphate is acceptable for use as a source of iron for dietary fortification, provided that the total intake of iron does not exceed the PMTDI. Products, including ferrous ammonium phosphate, that are intended to provide a source of additional iron should not be consumed by individuals with any type of iron storage disease, except under medical supervision.
Glycerol ester of gum rosin (GEGR)	N, T	The Committee decided to include GEGR in the ADI for glycerol esters of wood rosin (GEWR) of 0–25 mg/kg bw, thereby establishing a group ADI of 0–25 mg/kg bw for GEWR and GEGR. The specifications for GEGR were made tentative pending the submission of infrared spectra that correspond to the commercially available products, data on the resin acid composition obtained with updated chromatographic techniques and additional information on methods that enable the identification of the individual glycerol esters of rosins and their differentiation. This information should be submitted by the end of 2010.
Glycerol ester of tall oil rosin (GETOR)	N, T	The Committee concluded in principle that the data from GEWR could be used in the evaluation of GETOR; however, the Committee did not have adequate information on the composition of GETOR, considering that the source material and production processes are different, which may result in different by-products. The Committee decided that it could not evaluate GETOR without additional information on its composition in order to clarify the extent and significance of any differences relative to other glycerol esters of rosins. The specifications for GETOR were made tentative pending the submission of infrared spectra that correspond to the commercially

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
		available products, data on the resin acid composition obtained with updated chromatographic techniques and additional information on methods that enable the identification of the individual glycerol esters of rosins and their differentiation. The Committee also requested information on the identity of the sulfur compounds in the commercial product. This information should be submitted by the end of 2010.
Lycopene from all sources		The Committee decided to revise the group ADI established at the sixty-seventh meeting and replace it with a group ADI "not specified" for lycopene from all sources when used as food colour. Hence, the previous group ADI of 0–0.5 mg/kg bw for lycopene has been withdrawn. The group ADI "not specified" applies to synthetic lycopene, lycopene derived from the fungus *Blakeslea trispora* and lycopene extract from tomato that comply with the specifications, when used in accordance with Good Manufacturing Practice.
Lycopene extract from tomato	N	The Committee established a group ADI "not specified" for synthetic lycopene, lycopene derived from the fungus *Blakeslea trispora* and lycopene extract from tomato, when used as food colour, that comply with the specifications, and when used in accordance with Good Manufacturing Practice.
Mineral oil (low and medium viscosity) class II and class III		The Committee was informed that finalization of the requested studies has been delayed. The Committee decided to further extend the temporary group ADI, but noted that the temporary group ADI will be withdrawn at the end of 2011 if the data are not submitted by that time.
Octenyl succinic acid (OSA) modified gum arabic	N	The Committee decided to allocate a temporary ADI "not specified" for OSA modified gum arabic used in the applications specified and in accordance with Good Manufacturing Practice. The ADI is temporary pending submission of data by the end of 2011 showing hydrolysis of OSA modified gum arabic to confirm the validity of using gum arabic data in the evaluation of OSA modified gum arabic.
Sodium hydrogen sulfate	R	The Committee allocated an ADI "not specified" for sodium hydrogen sulfate, in line with the principles established for ionizable

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
		salts at its twenty-ninth meeting, when used in the applications specified and in accordance with Good Manufacturing Practice. Specifications were revised to include a new technological use.
Sucrose oligoesters (SOE) type I and type II	N	The Committee considered it appropriate to include SOE type I and type II in a group ADI of 0–30 mg/kg bw for sucrose esters of fatty acids, sucroglycerides and SOE type I and type II. The Committee emphasized that this evaluation is valid only for the material as specified.

[a] N, new specifications prepared; R, existing specifications revised; T, tentative specifications.

[b] ADI "not specified" is used to refer to a food substance of very low toxicity that, on the basis of the available data (chemical, biochemical, toxicological and other) and the total dietary intake of the substance arising from its use at the levels necessary to achieve the desired effects and from its acceptable background levels in food, does not, in the opinion of the Committee, represent a hazard to health. For that reason, and for the reasons stated in the individual evaluations, the establishment of an ADI expressed in numerical form is not deemed necessary. An additive meeting this criterion must be used within the bounds of Good Manufacturing Practice, i.e. it should be technologically efficacious and should be used at the lowest level necessary to achieve this effect, it should not conceal food of inferior quality or adulterated food, and it should not create a nutritional imbalance.

2. *FOOD ADDITIVES CONSIDERED FOR SPECIFICATIONS ONLY*

Food additive	Specifications[a]
Diacetyltartaric and fatty acid esters of glycerol	R
Ethyl lauroyl arginate	R
Glycerol ester of wood rosin	R, T
Nisin preparation	R
Nitrous oxide	R, T
Pectins	R
Starch sodium octenyl succinate	R
Tannic acid	R
Titanium dioxide	R
Triethyl citrate	R

[a] R, existing specifications revised; T, tentative specifications.

This volume contains monographs prepared at the seventy-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA), which met in Geneva, Switzerland, from 16 to 24 June 2009.

The toxicological monographs in this volume summarize the safety data on a number of food additives: branching glycosyltransferase from *Rhodothermus obamensis* expressed in *Bacillus subtilis*, cassia gum, ferrous ammonium phosphate, glycerol ester of gum rosin, glycerol ester of tall oil rosin, lycopene from all sources, octenyl succinic acid modified gum arabic, sodium hydrogen sulfate and sucrose oligoesters type I and type II. A monograph on the assessment of dietary exposure to cyclamic acid and its salts is also included.

This volume and others in the WHO Food Additives series contain information that is useful to those who produce and use food additives and veterinary drugs and those involved with controlling contaminants in food, government and food regulatory officers, industrial testing laboratories, toxicological laboratories and universities.

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WHO Technical Report Series
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EVALUATION OF CERTAIN FOOD ADDITIVES

Seventy-first report of the Joint FAO/WHO Expert Committee on Food Additives

Food and Agriculture Organization of the United Nations

World Health Organization

World Health Organization

WHO Technical Report Series
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Monographs containing summaries of relevant data and toxicological evaluations are available from WHO under the title:

Safety evaluation of certain food additives. WHO Food Additives Series, No. 62, 2010.

Specifications are issued separately by FAO under the title:

Compendium of food additive specifications. FAO JECFA Monographs 7, 2009.

1. Introduction

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) met in Geneva from 16 to 24 June 2009. The meeting was opened by Dr Keiji Fukuda, Assistant Director General ad interim, Health Security and Environment Cluster of the World Health Organization (WHO), on behalf of the Directors General of the Food and Agriculture Organization of the United Nations (FAO) and WHO. Dr Fukuda noted the more than 50 years of successful work of the Committee and emphasized the role that the Committee plays in improving and guaranteeing the safety of the global food supply, by providing independent scientific advice as a basis for food standards. As a result of the increasing globalization of food trade, illustrated by last year's melamine food contamination incident, this work is of increasing importance. Dr Fukuda emphasized that work on the provision of international scientific advice on food safety and other related topics remains an important and high priority for FAO and WHO. The Committee was then welcomed by Dr Jørgen Schlundt, Director of the Department of Food Safety and Zoonoses of WHO, who explained recent organizational changes within WHO to reinforce the department's ability to better reflect the farm-to-table approach for food safety assurance.

1.1 Declarations of interests

The Secretariat informed the Committee that all experts participating in the seventy-first meeting had completed declaration of interest forms and that no conflicts had been identified. The following declared interests and potential conflicts were discussed by the Committee. Professor Ron Walker had consulted in the past on some safety aspects for crystalline lycopene and hence did not participate in the discussions on the subject. Dr Brian Whitehouse declared that he had provided consultations for the preparation of a dossier for octenyl succinic acid modified gum arabic. The Committee decided that Dr Whitehouse would not participate in the discussions on this substance.

2. General considerations

As a result of the recommendations of the first Joint FAO/WHO Conference on Food Additives, held in September 1955 (*1*), there have been 70 previous meetings of the Committee (Annex 1). The present meeting was convened on the basis of a recommendation made at the sixty-ninth meeting (Annex 1, reference *190*).

The tasks before the Committee were:

— to elaborate further principles for evaluating the safety of food additives (section 2);

— to undertake toxicological evaluations of certain food additives (section 3 and Annex 2);

— to review and prepare specifications for certain food additives (section 3 and Annex 2).

2.1 Modification of the agenda

The Committee considered the names of the compounds branching enzyme from *Rhodothermus obamensis* and expressed in *Bacillus subtilis*, lycopene oleoresin extract from tomato and OSA (octenyl succinic acid)-modified acacia gum (gum arabic), which were on the agenda for evaluation for the first time, to be inappropriate. The Committee renamed them, respectively, branching glycosyltransferase from *Rhodothermus obamensis* expressed in *Bacillus subtilis*, lycopene extract from tomato and octenyl succinic acid modified gum arabic.

A temporary acceptable daily intake (ADI) "not specified" was allocated to the food additive cyclotetraglucose and cyclotetraglucose syrup at the sixty-eighth meeting of the Committee (Annex 1, reference *187*) pending submission of information on the identity of the bacterial strain used to produce the 6-α-glucosyltransferase and α-isomaltosyltransferase (6-GT/IMT) enzyme preparation and evidence of its lack of pathogenicity and toxicogenicity. The specifications for cyclotetraglucose syrup were made tentative pending additional information on the total saccharide content and test methods and on

the unidentified saccharide fraction. The Committee received the information requested, and the substances were therefore added to the agenda.

The Committee made recommendations at its sixty-fifth and sixty-seventh meetings (Annex 1, references *178* and *184*) regarding the need to re-evaluate certain alkane hydrocarbon solvents, particularly hexanes, as it was noted that products in commerce could differ from the material originally evaluated. As the recommendations were not sufficiently clear as to the scope of the re-evaluation to be undertaken, the Committee decided to add this item to the agenda with the aim to provide further clarification. In addition, during the evaluation of lycopene extract from tomato, it became apparent that the assessment of this extract depends on the evaluation of lycopene from all sources. Therefore, the Committee decided to add lycopene from all sources to the agenda.

The food additives ethyl lauroyl arginate, pectins, titanium dioxide and triethyl citrate were added to the agenda for minor revisions of specifications. The specifications monograph for glycerol ester of wood rosin was revised as a result of the evaluation of two additional glycerol esters of rosins at the present meeting.

2.2 Report from the forty-first session of the Codex Committee on Food Additives (CCFA)

The Chairperson of the Codex Committee on Food Additives (CCFA), Dr Junshi Chen, informed the Committee of the main achievements and outcomes of the forty-first session of CCFA (Shanghai, China, 16–20 March 2009), including details on texts forwarded to the thirty-second session of the Codex Alimentarius Commission (CAC) for adoption.

Dr Chen briefly summarized the decisions taken by the forty-first session of CCFA related to the recommendations of the sixty-ninth meeting of JECFA (Annex 1, reference *190*) and described the status of development of the Codex General Standard for Food Additives (GSFA). In view of the amount of work still necessary for its completion, the next session of CCFA will consider ways to expedite work on the GSFA. The Committee was informed that CCFA had completed work on inconsistencies identified between the names of the substances listed in the International Numbering System (INS) and in the Codex Specifications for Identity and Purity of Food Additives. In order to prevent more inconsistencies in the future, CCFA recommended that JECFA carefully consider the names of compounds listed in the INS for use in the specifications and, when they are considered not to be appropriate, to clearly indicate the reasons in order to facilitate follow-up actions by CCFA. A series of specific requests, included in the report of the forty-first session of CCFA, would be addressed by JECFA in a future meeting.

Finally, the forty-first session of CCFA agreed to a priority list of compounds for evaluation/re-evaluation by JECFA and also agreed to revise the text of the Circular Letter on Priority List of Food Additives Proposed for Evaluation by JECFA to allow an indication of the names of the country either where the compound is legally traded or where it has been approved and to include more details on data to be submitted by JECFA.

2.3 Principles governing the evaluation of compounds on the agenda

In making recommendations on the safety of food additives, the Committee took into consideration the principles established and contained in Environmental Health Criteria, No. 70 (EHC 70), *Principles for the safety assessment of food additives and contaminants in food* (Annex 1, reference *76*), as well as the principles elaborated subsequently at a number of its meetings (Annex 1, references *77*, *83*, *88*, *94*, *107*, *116*, *122*, *131*, *137*, *143*, *149*, *152*, *154*, *160*, *166*, *173*, *176*, *178*, *184*, *187* and *190*), including the present one. EHC 70 contains the most important observations, comments and recommendations made, up to the time of its publication, by the Committee and associated bodies in their reports on the safety assessment of food additives.

2.3.1 *Codex GSFA-related questions*

The Committee received two questions from the United States of America (USA), which arose when the USA was preparing a paper on the Codex GSFA for the next session of CCFA.

Sodium and potassium sulfates

The Committee was asked whether the ADI for sodium sulfate also applied to sodium hydrogen sulfate and whether the ADI for potassium sulfate also covered potassium hydrogen sulfate. The Committee had previously evaluated sodium and potassium sulfate; the sulfate ion was allocated an ADI "not specified" at the twenty-ninth meeting (Annex 1, reference *70*). In evaluating sodium hydrogen sulfate at the present meeting, the Committee considered that the principles elaborated at the twenty-ninth meeting for fully ionizable salts were applicable. It further considered that this approach could also be used in evaluating other fully ionizable sulfates, including food-grade potassium sulfate and potassium hydrogen sulfate. In conclusion, the ADI "not specified" for potassium sulfate is also applicable to potassium hydrogen sulfate.

Nisin and nisin preparation

In response to the question as to whether the ADI refers to nisin or nisin preparation, the Committee noted that when the name had been changed from

nisin to nisin preparation at the sixty-eighth meeting of the Committee (Annex 1, reference *187*), no modification was made that would impact the ADI. The Committee at this meeting, after reconsideration, decided to rename the specifications monograph "nisin" (see section 3.2.4).

The Committee also considered the question on a reporting basis for the nisin maximum levels in the Codex GSFA. It was noted that the ADI is expressed based on activity (units/kg body weight [bw]) for nisin and that the activity of individual commercial products may vary significantly.

2.3.2 *JECFA periodic re-evaluation of food additives*

JECFA has repeatedly noted the importance of reviewing substances previously evaluated when new data on those substances become available and in light of further developments in science and risk assessment methodologies. This was brought to the attention of the forty-first session of CCFA (*2*), which requested the JECFA Secretariat to prepare a discussion paper on the topic for consideration at the next session of CCFA.

The JECFA Secretariat presented to the Committee a draft discussion paper on the periodic review of JECFA evaluations of food additives for brief consideration and comments. The paper indicated that, since its establishment, JECFA has evaluated more than 600 food additives (excluding flavouring agents) and that approximately 30% of JECFA evaluations are more than 30 years old. The periodic review mechanisms established by the Codex Committee on Pesticide Residues (CCPR) for pesticide residue evaluations carried out by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) and the ongoing re-evaluation of food additives by the European Food Safety Authority (EFSA) were also noted.

The Committee noted that many re-evaluations have already been undertaken, based on specific requests from Member States and CAC, and considered that it will be necessary to develop criteria for a periodic review of substances. Criteria that may trigger a review have already been published in EHC 70, and revised criteria will be published in the updated principles and methods document, which is currently being finalized. These may serve as a basis for further consideration, and the revised criteria are repeated here:

> Periodic review of past decisions on safety is made necessary by one or more of the following developments:
>
> - a new manufacturing process for the food additive;
> - a new specification;
> - new data on the biological properties of the compound;
> - new data concerning the nature and/or the biological properties of the impurities present in a food additive;

- advances in scientific knowledge relevant to the nature or mode of action of food additives;
- changes in consumption patterns or level of use of a food additive; and
- improved requirements for safety evaluation. This is made possible by new scientific knowledge and the quality and quantity of safety data considered necessary in the case of food additives and residues of pesticides and veterinary drugs.

The Committee further noted that it is important to take existing assessments into account in the re-evaluation of a food additive and that a process must be developed by which the information needed for the re-evaluation can be provided.

2.3.3 *Data adjustment using food frequency questionnaires to better account for long-term dietary exposure*

Risk characterizations for long-term toxicity compare dietary exposure estimates with the relevant health-based values established for a lifetime. In previous meetings, the Committee often raised the fact that the use of short-term food consumption data to represent long-term dietary habits could lead to an overestimation of the amount of food consumed per day, in particular for foods consumed infrequently.

Typically, chronic dietary exposures are based on food consumption data collected over a period of 1–7 days. The use of surveys of duration longer than 1 day allows the averaging of the amount of food consumed per day to give the amount usually consumed. This will reduce the overestimation of the dietary exposure for chemicals occurring in foods consumed infrequently.

During the current meeting, the Committee examined a submission for an additive for which the "usual" food consumption data collected over a period of 2 days had been adjusted to better describe long-term dietary exposures by the use of food frequency questionnaires that estimated the number of eating occasions for each food over a period of 30 days for a comparable population. In this case, data from the 2003–2004 National Health and Nutrition Examination Survey (NHANES), which reports 2 days of food consumption, had been combined with data from the NHANES III 30-day food frequency survey for the population in the USA.

To better assess chronic dietary exposure, the Committee recommends the use of food consumption data collected over a period of more than 1 day with an averaging of the amounts of food consumed per day. Moreover, the Committee recommends that food consumption data collected over a few days be adjusted by using food frequency questionnaires on a comparable population where these data are available. This approach would better represent long-term consumption for foods consumed infrequently. The

Committee noted, however, that the food categories covered by a food frequency questionnaire are necessarily less numerous and far broader than those in a food recall or record survey. It would be simpler to apply this frequency adjustment to broad food categories (e.g. seafood) rather than to very specific ones (e.g. chocolate-filled biscuit). However, even in the latter case, the number of eating occasions recalled or recorded for the detailed food category could be adjusted relative to the number of eating occasions per month from the broad category.

2.3.4 *Guidelines for the safety evaluation of enzymes produced by genetically modified microorganisms*

At its sixty-fifth meeting (Annex 1, reference *178*), the Committee concluded that guidelines need to be developed on the safety evaluation of enzymes produced by genetically modified microorganisms (GMMs). At the sixty-eighth meeting (Annex 1, reference *187*), the Committee noted the ongoing international initiatives to elaborate guidelines for the safety evaluation of enzymes (including those from GMMs) and microorganisms intended for food applications. At the present meeting, the Committee discussed the new regulation for enzymes enacted by the European Parliament (*3*) and related guidance documents (*4*, *5*).

The Committee decided to update the General Specifications and Considerations for Enzymes Used in Food Processing (*6*) to expand recommendations for microbiology and molecular biology information to be submitted in dossiers for enzymes from microorganisms (including those from GMMs) and to discuss toxicological and other safety studies for enzymes from all sources.

The Committee recommended that the JECFA Secretariat establish a working group to update the current guidance document on enzymes for discussion at a future meeting.

2.4 Hexanes

At the sixty-fifth and sixty-seventh meetings of the Committee (Annex 1, references *178* and *184*), it was noted that the specifications for hexanes should be revised, as the material of commerce, a light petroleum fraction, was a mixture of components of different chain lengths with potential differences in toxicity. At the current meeting, the Committee was made aware that there were new data on the toxicity of *n*-hexane and that the composition of commercially available solvents containing *n*-hexane may not comply with the existing specifications. The Committee concluded that these new data indicate that the specifications and toxicity of hexanes should be reconsidered at a future meeting and reiterated the recommendations made in this regard at the sixty-fifth and sixty-seventh meetings.

3. Specific food additives

The Committee evaluated nine food additives for the first time and re-evaluated a number of others. Information on the safety evaluations and on specifications is summarized in Annex 2. Details of further toxicological studies and other information required for certain substances are given in Annex 3.

3.1 Safety evaluations

3.1.1 *Branching glycosyltransferase from* Rhodothermus obamensis *expressed in* Bacillus subtilis

Explanation

At the request of CCFA at its fortieth session (*7*), the Committee evaluated the enzyme branching glycosyltransferase (1,4-α-glucan branching enzyme; Enzyme Commission number 2.4.1.18), which it had not evaluated previously. Branching glycosyltransferase catalyses the transfer of a segment of a 1,4-α-D-glucan chain to a primary hydroxy group in a similar glucan chain to create 1,6-linkages. The enzyme is intended for use in starch processing to obtain modified starch with an increased number of branch points and improved functional properties.

Genetic modification

Branching glycosyltransferase is manufactured by pure culture fermentation of a genetically modified strain of *Bacillus subtilis* containing a synthetic gene coding for branching glycosyltransferase from *Rhodothermus obamensis*. *Bacillus subtilis* is a Gram-positive bacterium that is widely distributed in nature and is considered to be non-pathogenic and non-toxigenic. It has a long history of use in the production of enzymes used in food processing, including enzymes from genetically engineered strains. It has also been granted a Qualified Presumption of Safety status by EFSA.

The gene encoding branching glycosyltransferase was originally cloned from *R. obamensis*, a thermophilic bacterium that was isolated from a marine

The Committee concluded that the estimated dietary exposure to OSA modified gum arabic from the proposed uses would be less than 20 mg/kg bw per day.

Evaluation

Only limited data were available for OSA modified gum arabic. The Committee concluded that the available data on OSA modified gum arabic indicate a very low toxicity, comparable with the toxicities of traditional gum arabic and starch sodium octenyl succinate (OSA modified food starch), both of which were previously reviewed by the Committee and allocated ADIs "not specified".

Comparing the exposure estimate of 20 mg/kg bw per day with the NOEL from the 90-day study of oral toxicity in rats (3410 mg/kg bw per day, the highest dose tested), the margin of exposure is at least 170. The Committee decided to allocate a temporary ADI "not specified" to OSA modified gum arabic, used in the applications specified and in accordance with Good Manufacturing Practice. The Committee decided to make the ADI temporary pending submission of data by the end of 2011 showing hydrolysis of OSA modified gum arabic to confirm the validity of using gum arabic data in the evaluation of OSA modified gum arabic.

A toxicological monograph was prepared. A Chemical and Technical Assessment and new specifications were prepared.

3.1.12 *Sodium hydrogen sulfate*

Explanation

At the present meeting, the Committee evaluated sodium hydrogen sulfate for use as an acidifier, at the request of CCFA at its fortieth session (*7*). The Committee was asked for a safety assessment and revision of specifications. At its sixty-eighth meeting, the Committee considered sodium hydrogen sulfate for use in the preparation of acidified sodium chlorite, an antimicrobial washing solution, and established specifications, but did not evaluate it for safety (Annex 1, reference *187*). At its ninth and twenty-third meetings, the Committee evaluated a large number of food acids and salts and was of the opinion that ADIs for ionizable salts should be based on previously accepted recommendations for the constituent cations and anions (Annex 1, references *11* and *50*).

The sulfate ion was evaluated at the twenty-ninth meeting of the Committee (Annex 1, reference *70*), when an ADI "not specified" was established, as sulfate is a natural constituent of food and is a product of sulfur metabolism

in animals. Sodium sulfate was evaluated at the fifty-third, fifty-fifth and fifty-seventh meetings (Annex 1, references *144*, *149* and *154*), when an ADI "not specified" was established.

Chemical and technical considerations

Sodium hydrogen sulfate is manufactured by mixing sodium chloride with sulfuric acid at elevated temperatures to form molten sodium hydrogen sulfate. The molten sodium hydrogen sulfate is sprayed and cooled to form a solid product with uniform particle size.

Toxicological data

When sodium hydrogen sulfate is added to food products containing water or after ingestion of sodium hydrogen sulfate, it ionizes to sodium ions, hydrogen ions and sulfate ions. The Committee received a submission containing unpublished studies on sodium hydrogen sulfate, including a study on its acute toxicity and studies on inhalation toxicity, skin irritation and corrosivity, and freshwater ecotoxicity. A literature search identified no published studies of the toxicity of sodium hydrogen sulfate. Additional information identified by a literature search related to sulfate, as the Committee decided to assess sodium hydrogen sulfate in terms of the sulfate component because of its dissociation to the constituent ions and given that sodium and hydrogen ions are ubiquitous and natural constituents of foods.

In an acute toxicity study, the oral LD_{50} of sodium hydrogen sulfate in rats was determined to be 2800 mg/kg bw in males and >2500 mg/kg bw in females. The additional studies received as part of the submission were not considered relevant to the evaluation of the oral toxicity of sodium hydrogen sulfate.

In studies evaluating the effect of inorganic sulfate on bowel function, the body weight and kidney weight of neonatal pigs administered up to 2000 mg/l in a liquid diet for 18 days were unaffected. In a 16-day study, the concentration of added sulfate in the diet at which 50% of the piglets developed non-pathogenic diarrhoea was estimated to be between 1600 and 1800 mg/l. No differences in bowel movements were noted in adult volunteers receiving sulfate in the drinking-water at concentrations up to 1200 mg/l for 3 consecutive days.

The additional studies identified on sulfate did not raise concern about its toxicity.

Assessment of dietary exposure

Sodium hydrogen sulfate is typically added to beverages, confectionery, fillings, syrups, processed cheeses, salad dressings, sauces, jams and jellies, and processed vegetable products at levels ranging from 500 to 4000 mg/kg. For beverages, sodium hydrogen sulfate is generally used in non-citrus-flavoured soft drinks, tea, and chocolate-flavoured and coffee-flavoured drinks, as it does not impart a sour or citric taste, as do other acidifiers.

Based on poundage data for the USA, where the food additive has the highest reported production levels, mean per capita exposures for the population in the USA for current production volumes and for increased production volumes in the future, as predicted by the sponsor, were estimated to be 20 and 50 mg/day, respectively, assuming that all members of the population were consumers of products containing the additive.

From the limited data submitted by the sponsor on the proposed use of sodium hydrogen sulfate as a food acid, potential mean and high-consumer dietary exposures (derived from consumption for two food groups with highest dietary exposure at the 95th percentile plus mean for population for all other food groups) for 19 European populations (aged 16–64 years) were calculated based on typical use levels, assuming that the additive was used in all foods in each of the broad food categories identified above. Potential mean per capita dietary exposures for this "worst case" scenario ranged from 400 to 1160 mg/day for the whole population and from 1090 to 6340 mg/day for high consumers of foods containing sodium hydrogen sulfate. Potential dietary exposures based on individual dietary records and use of sodium hydrogen sulfate in food subcategories specified by the sponsor were submitted for the Australian population. Potential mean dietary exposures for Australians were lower than those for Europeans but of the same order of magnitude (mean per capita dietary exposure of 700 mg/day for the whole Australian population and 1210 mg/day for high consumers at the 90th percentile). The Committee considered that the predicted dietary exposures for the European and Australian populations were overestimates, a view supported by the much lower per capita estimates reported for the population in the USA. The actual use of sodium hydrogen sulfate would be restricted to subcategories within the broader food group and to foods within these subcategories where a low pH was required and/or for drinks where an acidic or citric taste was undesirable.

Evaluation

Considering that the available evidence did not provide any indication of toxicity, the Committee allocated an ADI "not specified" for sodium hydrogen sulfate, in line with the principles established for ionizable salts at its

twenty-ninth meeting, when used in the applications specified and in accordance with Good Manufacturing Practice.

A toxicological monograph was prepared. Specifications were revised to include the new technological use. A Chemical and Technical Assessment for sodium hydrogen sulfate was prepared.

3.1.13 *Sucrose oligoesters type I and type II*

Explanation

At the request of CCFA at its thirty-ninth session (*10*), the Committee evaluated sucrose oligoesters (SOE), which are separated into two types, SOE type I and type II. SOE type I and type II are produced by interesterification of sucrose with methyl esters of fatty acids derived from edible fats and oils, including hydrogenated fats and oils such as stearic acid and palmitic acid. A sucrose molecule has eight hydroxyl groups, and so it can produce mono- to octa-esters (Table 2). "Sucrose esters of fatty acids" consist mainly of sucrose mono- to tri-esters, whereas SOE type I consists mainly of sucrose tetra- to octa-esters and SOE type II consists of sucrose mono- to octa-esters. The lipophilic character of these constituents increases according to the increasing degree of esterification and the increasing chain length of the fatty acids. Other physical and chemical properties of the products also vary depending on the degree of esterification and the chain length of the fatty acids.

Table 2.
Classification of sucrose fatty acid esters

Property	Group	Composition of esters (%)			
		Mono–tri	Tetra–octa	Hepta+octa	Octa
Hydrophilic	Sucrose esters of fatty acids	80–100	0–20	–	–
↓	Sucrose oligoesters type II	20–80	20–80	0–20	0–10
↓	Sucrose oligoesters type I	0–20	80–100	0–50	0–20
Lipophilic	Olestra[a]	–	–	97–100	70–100

[a] The monograph for olestra in the sixth edition of the Food Chemicals Codex specifies the following distribution for the number of esters: octa-esters, not less than 70%; hexa-, hepta- and octa-esters, not less than 97%; hexa-esters, not more than 1%; and penta-esters, not more than 0.5%. Olestra is used as a replacement for fats in food.

SOE type I and type II are lipophilic emulsifiers as well as stabilizers and tableting aids for foods presented in tablet form. They are authorized for use in a number of countries, including Japan, the USA, China and the Republic of Korea.

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Annex 1

Reports and other documents resulting from previous meetings of the Joint FAO/WHO Expert Committee on Food Additives

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2. *Procedures for the testing of intentional food additives to establish their safety for use* (Second report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Report Series, No. 17, 1958; WHO Technical Report Series, No. 144, 1958 (out of print).
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Annex 2

Acceptable daily intakes, other toxicological information and information on specifications

1. Food additives evaluated

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
Branching glycosyltransferase from *Rhodothermus obamensis* expressed in *Bacillus subtilis*	N	The Committee allocated an **ADI "not specified"** for branching glycosyl-transferase from *Rhodothermus obamensis* expressed in *Bacillus subtilis* used in the specified applications and in accordance with Good Manufacturing Practice.
Cassia gum	N, T	The Committee allocated an **ADI "not specified"** for cassia gum that complies with the tentative specifications established at the current meeting, when used in the applications specified and in accordance with Good Manufacturing Practice. The Committee decided to make the specifications tentative pending submission of data on a suitable and validated method for determination of anthraquinones at a level of 0.5 mg/kg and below, by the end of 2010.
Cyclamic acid and its salts (dietary exposure assessment)		Of the four maximum use levels (250, 500, 750 and 1000 mg/kg) that the Committee considered at the request of CCFA for cyclamates in beverages covered by Codex GSFA Food Category 14.1.4, only the lowest level of 250 mg/kg was not likely to lead to dietary exposures exceeding the ADI for high consumers, including children. Moreover, it was noted that a maximum use level of 350 mg/kg also resulted in dietary exposures for high consumers, including children, that were less than the ADI.

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
Cyclotetraglucose and cyclotetraglucose syrup	R (cyclotetraglucose syrup)	The Committee established an **ADI "not specified"** for cyclotetraglucose and cyclotetraglucose syrup. The specifications for cyclotetraglucose syrup were revised, and the tentative designation was removed.
Ferrous ammonium phosphate	N	The newly available information on the toxicity of iron did not indicate a need to revise the PMTDI of 0.8 mg/kg bw. Consideration of the toxicity of ammonium and phosphate did not indicate a need to revise the Committee's previous evaluations of these ions. The Committee concluded that ferrous ammonium phosphate is acceptable for use as a source of iron for dietary fortification, provided that the total intake of iron does not exceed the PMTDI. Products, including ferrous ammonium phosphate, that are intended to provide a source of additional iron should not be consumed by individuals with any type of iron storage disease, except under medical supervision.
Glycerol ester of gum rosin (GEGR)	N, T	The Committee decided to include GEGR in the ADI for GEWR of 0–25 mg/kg bw, thereby establishing a **group ADI of 0–25 mg/kg bw** for GEWR and GEGR. The specifications for GEGR were made tentative pending the submission of infrared spectra that correspond to the commercially available products, data on the resin acid composition obtained with updated chromatographic techniques, and additional information on methods that enable the identification of the individual glycerol esters of rosins and their differentiation. This information should be submitted by the end of 2010.
Glycerol ester of tall oil rosin (GETOR)	N, T	The Committee concluded in principle that the data from GEWR could be used in the evaluation of GETOR; however, the Committee did not have adequate information on the composition of GETOR, considering that the source material and production processes are

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
		different, which may result in different by-products. The Committee decided that it could not evaluate GETOR without additional information on its composition in order to clarify the extent and significance of any differences relative to other glycerol esters of rosins. The specifications for GETOR were made tentative pending the submission of infrared spectra that correspond to the commercially available products, data on the resin acid composition obtained with updated chromatographic techniques, and additional information on methods that enable the identification of the individual glycerol esters of rosins and their differentiation. The Committee also requested information on the identity of the sulfur compounds in the commercial products. This information should be submitted by the end of 2010.
Lycopene from all sources		The Committee decided to revise the group ADI established at the sixty-seventh meeting and replace it with a **group ADI "not specified"** for lycopene from all sources when used as a food colour. Hence, the previous group ADI of 0–0.5 mg/kg for lycopene has been withdrawn. The group ADI "not specified" applies to synthetic lycopene, lycopene derived from the fungus *Blakeslea trispora* and lycopene extract from tomato that comply with the specifications, when used in accordance with Good Manufacturing Practice.
Lycopene extract from tomato	N	The Committee established a **group ADI "not specified"** for synthetic lycopene, lycopene derived from the fungus *Blakeslea trispora* and lycopene extract from tomato, when used as a food colour, that comply with the specifications, and when used in accordance with Good Manufacturing Practice.
Mineral oil (low and medium viscosity) class II and class III		The Committee was informed that finalization of the requested studies has been delayed. The Committee decided to

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
		further **extend the temporary group ADI**, but noted that the temporary group ADI will be withdrawn at the end of 2011 if the data are not submitted by that time.
Octenyl succinic acid (OSA) modified gum arabic	N	The Committee decided to allocate a **temporary ADI "not specified"** for OSA modified gum arabic used in the applications specified and in accordance with Good Manufacturing Practice. The ADI is temporary pending submission of data by the end of 2011 showing hydrolysis of OSA modified gum arabic to confirm the validity of using gum arabic data in the evaluation of OSA modified gum arabic.
Sodium hydrogen sulfate	R	The Committee allocated an **ADI "not specified"** for sodium hydrogen sulfate, in line with the principles established for ionizable salts at its twenty-ninth meeting, when used in the applications specified and in accordance with Good Manufacturing Practice. Specifications were revised to include a new technological use.
Sucrose oligoesters (SOE) type I and type II	N	The Committee considered it appropriate to include SOE type I and type II in a **group ADI of 0–30 mg/kg bw** for sucrose esters of fatty acids, sucroglycerides and SOE type I and type II. The Committee emphasized that this evaluation is valid only for the material as specified.

[a] N, new specifications prepared; R, existing specifications revised; T, tentative specifications.

[b] ADI "not specified" is used to refer to a food substance of very low toxicity that, on the basis of the available data (chemical, biochemical, toxicological and other) and the total dietary intake of the substance arising from its use at the levels necessary to achieve the desired effects and from its acceptable background levels in food, does not, in the opinion of the Committee, represent a hazard to health. For that reason, and for the reasons stated in the individual evaluations, the establishment of an ADI expressed in numerical form is not deemed necessary. An additive meeting this criterion must be used within the bounds of Good Manufacturing Practice, i.e. it should be technologically efficacious and should be used at the lowest level necessary to achieve this effect, it should not conceal food of inferior quality or adulterated food, and it should not create a nutritional imbalance.

2. Food additives considered for specifications only

Food additive	Specifications[a]
Diacetyltartaric and fatty acid esters of glycerol	R
Ethyl lauroyl arginate	R
Glycerol ester of wood rosin	R, T
Nisin preparation	R
Nitrous oxide	R, T
Pectins	R
Starch sodium octenyl succinate	R
Tannic acid	R
Titanium dioxide	R
Triethyl citrate	R

[a] R, existing specifications revised; T, tentative specifications.

Annex 3

Further information required or desired

Cassia gum

Information is required on a suitable and validated method for determination of anthraquinones in cassia gum at a level of 0.5 mg/kg and below. This information should be submitted by the end of 2010.

Glycerol ester of gum rosin

The Committee requested that it be provided with full reports of the two 90-day toxicity studies with GEGR in rats fed dietary concentrations of up to 1.0% to confirm the validity of the comparison of GEWR with GEGR.

The specifications were made tentative pending the submission of infrared spectra that correspond to the commercially available products, data on the resin acid composition obtained with updated chromatographic techniques, and additional information on methods that enable the identification of the individual glycerol esters of rosins and their differentiation. This information should be submitted by the end of 2010.

Glycerol ester of tall oil rosin

The Committee did not have adequate information on the composition of GETOR, as the source material and production processes are different, which may result in different by-products. Therefore, the Committee decided that it could not evaluate GETOR without additional information on the composition of GETOR in order to clarify the extent and significance of any differences relative to other glycerol esters of rosins.

The specifications were made tentative pending the submission of infrared spectra that correspond to the commercially available products, data on the resin acid composition obtained with updated chromatographic techniques, and additional information on methods that enable the identification of the individual glycerol esters of rosins and their differentiation. The Committee also requested information on the identity of the sulfur compounds in the commercial products. This information should be submitted by the end of 2010.

Glycerol ester of wood rosin

The specifications were made tentative pending the submission of infrared spectra that correspond to the commercially available products, data on the resin acid composition obtained with updated chromatographic techniques, and additional information on methods that enable the identification of the individual glycerol esters of rosins and their differentiation. This information should be submitted by the end of 2010.

Mineral oil (low and medium viscosity) class II and class III

The Committee at its current meeting was informed that studies are under way but that technical problems had been encountered that will delay the finalization of the requested studies. The Committee received confidential information on the studies and nature of the problems and, based on this, decided to further extend the temporary group ADI. The Committee noted that the temporary group ADI will be withdrawn at the end of 2011 if the data are not submitted by that time.

Nitrous oxide

The revised specifications were made tentative, as information on a capillary gas chromatographic assay method was required. This information should be submitted by the end of 2010.

Octenyl succinic acid modified gum arabic

The ADI is temporary pending submission of data by the end of 2011 showing hydrolysis of OSA modified gum arabic to confirm the validity of using gum arabic data in the evaluation of OSA modified gum arabic.

This report represents the conclusions of a Joint FAO/WHO Expert Committee convened to evaluate the safety of various food additives, with a view to recommending acceptable daily intakes (ADIs) and to preparing specifications for identity and purity.

The first part of the report contains a general discussion of the principles governing the toxicological evaluation and assessment of intake of food additives. A summary follows of the Committee's evaluations of technical, toxicological and intake data for certain food additives: branching glycosyltransferase from *Rhodothermus obamensis* expressed in *Bacillus subtilis*, cassia gum, cyclamic acid and its salts (dietary exposure assessment), cyclotetraglucose and cyclotetraglucose syrup, ferrous ammonium phosphate, glycerol ester of gum rosin, glycerol ester of tall oil rosin, lycopene from all sources, lycopene extract from tomato, mineral oil (low and medium viscosity) class II and class III, octenyl succinic acid modified gum arabic, sodium hydrogen sulfate and sucrose oligoesters type I and type II.

Specifications for the following food additives were revised: diacetyltartaric acid and fatty acid esters of glycerol, ethyl lauroyl arginate, glycerol ester of wood rosin, nisin preparation, nitrous oxide, pectins, starch sodium octenyl succinate, tannic acid, titanium dioxide and triethyl citrate.

Annexed to the report are tables summarizing the Committee's recommendations for intakes and toxicological evaluations of the food additives considered.

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Appendix VII: EPISuite™ 4.0 modeling Results

```
CAS Number: 7681-38-1
SMILES : O([Na])S(=O)(=O)O
CHEM   : SULFURIC ACID, MONOSODIUM SALT
MOL FOR: H1 O4 S1 Na1
MOL WT : 120.06
---------------------------- EPI SUMMARY (v4.10) -------------------------
 Physical Property Inputs:
    Log Kow (octanol-water):   ------
    Boiling Point (deg C)  :   ------
    Melting Point (deg C)  :   ------
    Vapor Pressure (mm Hg) :   ------
    Water Solubility (mg/L):   ------
    Henry LC (atm-m3/mole) :   ------

 Log Octanol-Water Partition Coef (SRC):
    *** WARNING: Inorganic Compound (Outside Estir
    Log Kow (KOWWIN v1.68 estimate) =  -6.85

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.43):
   *** WARNING: Inorganic Compound (Outside Estimate Domain) ***
   *** WARNING: Estimations NOT VALID ***
    Boiling Pt (deg C):  824.58  (Adapted Stein & Brown method)
    Melting Pt (deg C):  349.84  (Mean or Weighted MP)
    VP(mm Hg,25 deg C):  1.51E-024  (Modified Grain method)
    VP (Pa, 25 deg C) :  2.01E-022  (Modified Grain method)
    Subcooled liquid VP: 7.72E-021 mm Hg (25 deg C, Mod-Grain method)
                       : 1.03E-018 Pa (25 deg C, Mod-Grain method)

 Water Solubility Estimate from Log Kow (WSKOW v1.42):
    *** WARNING: Inorganic Compound (Outside Estimation Domain)**
    Water Solubility at 25 deg C (mg/L):  1e+006
       log Kow used: -6.85 (estimated)
       no-melting pt equation used

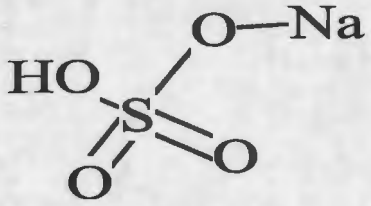
 Water Sol Estimate from Fragments:
    *** WARNING: Inorganic Compound (Outside Estimation Domain)***
    *** WARNING: Wat Sol Estimation NOT Valid ***
    Wat Sol (v1.01 est) =  1e+006 mg/L

 ECOSAR Class Program (ECOSAR v1.00):
    Class(es) found:
       Neutral Organics

 Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
   *** WARNING: Inorganic Compound (Outside Estimation Domain) **
   *** WARNING: Estimation NOT VALID **
   Bond Method :   2.55E-011  atm-m3/mole  (2.58E-006 Pa-m3/mole)
   Group Method:   Incomplete
 For Henry LC Comparison Purposes:
   User-Entered Henry LC:  not entered
   Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
      HLC:  2.385E-031 atm-m3/mole  (2.417E-026 Pa-m3/mole)
      VP:   1.51E-024 mm Hg (source: MPBPVP)
      WS:   1E+006 mg/L (source: WSKOWWIN)

 Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
   *** WARNING: Inorganic Compound (Outside Estimation Domain)**
   *** WARNING: Estimation NOT VALID ***
  Log Kow used:  -6.85  (KowWin est)
  Log Kaw used:  -8.982  (HenryWin est)
      Log Koa (KOAWIN v1.10 estimate):  2.132
      Log Koa (experimental database):  None

 Probability of Rapid Biodegradation (BIOWIN v4.10):
    *** WARNING: Inorganic Compound (Outside Estimation Domain)**
    *** WARNING: Estimation NOT VALID ***
   Biowin1 (Linear Model)          :   0.7009
```



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  Biowin2 (Non-Linear Model)     :   0.8343
Expert Survey Biodegradation Results:
  Biowin3 (Ultimate Survey Model):   2.9824  (weeks       )
  Biowin4 (Primary Survey Model) :   3.7062  (days-weeks  )
MITI Biodegradation Probability:
  Biowin5 (MITI Linear Model)    :   0.4204
  Biowin6 (MITI Non-Linear Model):   0.4242
Anaerobic Biodegradation Probability:
  Biowin7 (Anaerobic Linear Model):  0.8361
Ready Biodegradability Prediction:   NO

Hydrocarbon Biodegradation (BioHCwin v1.01):
    Structure incompatible with current estimation method!

 Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
  Vapor pressure (liquid/subcooled):  1.03E-018 Pa (7.72E-021 mm Hg)
  Log Koa (Koawin est  ): 2.132
   Kp (particle/gas partition coef. (m3/ug)):
       Mackay model           :  2.91E+012
       Octanol/air (Koa) model:  3.33E-011
   Fraction sorbed to airborne particulates (phi):
       Junge-Pankow model     :  1
       Mackay model           :  1
       Octanol/air (Koa) model:  2.66E-009

 Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
    *** WARNING: Inorganic Compound (Outside Estimation Domain)***
   Hydroxyl Radicals Reaction:
      OVERALL OH Rate Constant =   0.1400 E-12 cm3/molecule-sec
      Half-Life =    76.400 Days (12-hr day; 1.5E6 OH/cm3)
   Ozone Reaction:
      No Ozone Reaction Estimation
   Fraction sorbed to airborne particulates (phi):
      1 (Junge-Pankow, Mackay avg)
      2.66E-009 (Koa method)
    Note: the sorbed fraction may be resistant to atmospheric oxidation

 Soil Adsorption Coefficient (KOCWIN v2.00):
   *** WARNING: Inorganic Coumpound (Outside Estimation Domain) **
   *** WARNING: Estimation NOT VALID **
      Koc    :  2.21  L/kg (MCI method)
      Log Koc:  0.344       (MCI method)
      Koc    :  0.001984  L/kg (Kow method)
      Log Koc:  -2.702      (Kow method)

 Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
    Rate constants can NOT be estimated for this structure!

 Bioaccumulation Estimates (BCFBAF v3.01):
   Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
   Log Biotransformation Half-life (HL) = -2.5211 days (HL = 0.003012 days)
   Log BCF Arnot-Gobas method (upper trophic) = -0.049 (BCF = 0.8931)
   Log BAF Arnot-Gobas method (upper trophic) = -0.049 (BAF = 0.8931)
       log Kow used: -2.20 (estimated)

 Volatilization from Water:
    Henry LC:  2.55E-011 atm-m3/mole  (estimated by Bond SAR Method)
    Half-Life from Model River: 2.516E+007  hours   (1.048E+006 days)
    Half-Life from Model Lake : 2.744E+008  hours   (1.144E+007 days)

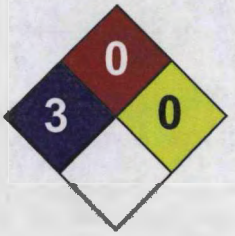
 Removal In Wastewater Treatment:
    Total removal:              1.85  percent
    Total biodegradation:       0.09  percent
    Total sludge adsorption:    1.75  percent
    Total to Air:               0.00  percent
      (using 10000 hr Bio P,A,S)
```

Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	1.52	1.83e+003	1000
Water	37.3	360	1000
Soil	61.1	720	1000
Sediment	0.0717	3.24e+003	0

Persistence Time: 545 hr

Appendix VIII: Sodium Bisulfate MSDS



Health	3
Fire	0
Reactivity	0
Personal Protection	J

Material Safety Data Sheet
Sodium bisulfate MSDS

Section 1: Chemical Product and Company Identification

Product Name: Sodium bisulfate

Catalog Codes: SLS2104, SLS4258

CAS#: 7681-38-1

RTECS: VZ1860000

TSCA: TSCA 8(b) inventory: Sodium bisulfate

CI#: Not available.

Synonym: GBS; Nitre cake; Sodium acid sulfate; Sodium pyrosulfate; Sodium hydrogen sulfate; Sulfuric acid, monosodium salt.

Chemical Name: Sodium Bisulfate

Chemical Formula: NaHSO4

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call: 1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Sodium bisulfate	7681-38-1	100

Toxicological Data on Ingredients: Sodium bisulfate: ORAL (LD50): Acute: 2800 mg/kg [Rat].

Section 3: Hazards Identification

Potential Acute Health Effects:
Very hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation. Hazardous in case of skin contact (corrosive, permeator). The amount of tissue damage depends on length of contact. Eye contact can result in comeal damage or blindness. Skin contact can produce inflammation and blistering. Inhalation of dust will produce irritation to gastro-intestinal or respiratory tract, characterized by burning, sneezing and coughing. Severe over-exposure can produce lung damage, choking, unconsciousness or death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:
CARCINOGENIC EFFECTS: Not available. MUTAGENIC EFFECTS: Mutagenic for bacteria and/or yeast. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available. Repeated exposure of the eyes to a low level of dust can produce eye irritation. Repeated skin exposure can produce local skin destruction, or dermatitis. Repeated inhalation of dust can produce varying degree of respiratory irritation or lung damage.

Section 4: First Aid Measures

Eye Contact:
Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention immediately.

Skin Contact:
In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Cold water may be used.Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:
Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek medical attention.

Inhalation:
If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Serious Inhalation:
Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. WARNING: It may be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek immediate medical attention.

Ingestion:
Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention if symptoms appear.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Not applicable.

Explosion Hazards in Presence of Various Substances:
Risks of explosion of the product in presence of mechanical impact: Not available. Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill: Use appropriate tools to put the spilled solid in a convenient waste disposal container.

Large Spill:
Corrosive solid. Stop leak if without risk. Do not get water inside container. Do not touch spilled material. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Call for assistance on disposal.

Section 7: Handling and Storage

Precautions:
Keep locked up.. Keep container dry. Do not ingest. Do not breathe dust. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as oxidizing agents, alkalis.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:
Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection:
Splash goggles. Synthetic apron. Vapor and dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:
Splash goggles. Full suit. Vapor and dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Granular solid.)

Odor: Not available.

Taste: Not available.

Molecular Weight: 120.6 g/mole

Color: Off-white.

pH (1% soln/water): Not available.

Boiling Point: Not available.

Melting Point: 157.22°C (315°F)

Critical Temperature: Not available.

Specific Gravity: 2.435 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility:

Easily soluble in hot water. Soluble in cold water. Soluble in 2 parts cold water. Soluble in 1 part boiling water. Decomposed by alcohol into sodium sulfate and free H2SO4.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials, moisture

Incompatibility with various substances: Reactive with oxidizing agents, alkalis.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity:
Do not mix with liquid chlorine bleach (hypochlorites), ammonia cleansers or similar products, or alcohols. Hygroscopic; keep container tightly closed.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Dermal contact. Inhalation. Ingestion.

Toxicity to Animals: Acute oral toxicity (LD50): 2800 mg/kg [Rat].

Chronic Effects on Humans: MUTAGENIC EFFECTS: Mutagenic for bacteria and/or yeast.

Other Toxic Effects on Humans:
Very hazardous in case of skin contact (irritant), of ingestion, of inhalation. Hazardous in case of skin contact (corrosive, permeator).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: May affect genetic material (mutagenic)

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: Can cause severe skin irritation or burns. Eyes: Can cause severe irritation or burns of the eyes. Inhalation: It is destructive to the mucous membranes of the upper respiratory tract. Causes irritation and chemical burns to the respiratory tract with burning pain in the nose and throat, coughing , wheezing, shortness of breath, and pulmonary edema. Inhalation may be fatal as a result of spasm, inflammation, edema of the larynx and bronchi, chemical pneumonitis, and pulmonary edema. Ingestion: Causes gastrointestinal tract irritation and burns. Symptoms may include nausea and vomiting. May cause severe and permanent damage to the digestive tract. Chronic Potential Health Effects: Repeated exposure may cause erosion of teeth, lung irritation, bronchitis, persistant coughing,

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The product itself and its products of degradation are not toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:
Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Class 8: Corrosive material

Identification: : Corrosive Solid, n.o.s.(Sodium Bisulfate) UNNA: 1759 PG: III

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:
Connecticut hazardous material survey.: Sodium bisulfate New Jersey: Sodium bisulfate TSCA 8(b) inventory: Sodium bisulfate

Other Regulations:
OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200). EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada): CLASS E: Corrosive solid.

DSCL (EEC):
R34- Causes burns. R41- Risk of serious damage to eyes. S24/25- Avoid contact with skin and eyes. S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S36/37/39- Wear suitable protective clothing, gloves and eye/face protection.

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 0

Reactivity: 0

Personal Protection: j

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 0

Reactivity: 0

Specific hazard:

Protective Equipment:
Gloves. Synthetic apron. Vapor and dust respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate. Splash goggles.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

Created: 10/10/2005 08:27 PM

Last Updated: 11/01/2010 12:00 PM

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Appendix IX: Cal DPR Sodium Bisulfate

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
SODIUM BISULFATE

Chemical Code # 905, Tolerance # 50263
December 20, 2002

I. DATA GAP STATUS[1]

Chronic toxicity, rat:	Data gap, no study on file
Chronic toxicity, dog:	Data gap, no study on file
Oncogenicity, rat:	Data gap, no study on file
Oncogenicity, mouse:	Data gap, no study on file
Reproduction, rat:	Data gap, no study on file
Teratology, rat:	Data gap, no study on file
Teratology, rabbit:	Data gap, no study on file
Gene mutation:	Data gap, no study on file
Chromosome effects:	Data gap, no study on file
DNA damage:	Data gap, no study on file
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.
[1] See notes on page 2.
All record numbers through 182475 examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
File name: T021220
Prepared by Gee, December 20, 2002

See the "Reregistration Eligibility Decision (RED)" of the Office of Prevention, Pesticides and Toxic Substances, US EPA, dated December, 1993, on "Mineral Acids" for further information.

There are 48 products currently registered in California containing sodium bisulfate. All of these

are registered as adjuvants (water modifiers) and/or as swimming pool/spa additives for pH adjustment, among other properties. Of the 48, 45 products carry the signal word "Danger" and 3 "Caution." (The RED indicates that sodium bisulfate can also be used as a disinfectant for toilet bowls.)

As stated in the RED of US EPA, sodium bisulfate yields sodium and sulfate, both common chemical entities in the environment. Sulfate salts are considered GRAS. There are no registered food uses for sodium bisulfate. US EPA, therefore, had no concern for dietary exposure in the 1993 RED.

Sodium bisulfate solutions at 60 - 70% active ingredient are category III for dermal exposure but I for eye irritation, hence the label precautions.

Based on the physical properties, uses and known break down products, no further studies are being required at this time.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

CHRONIC TOXICITY, RAT

No study on file.

CHRONIC TOXICITY, DOG

No study on file.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

No study on file.

TERATOLOGY, RABBIT

No study on file.

GENE MUTATION

No study on file.

CHROMOSOME EFFECTS

No study on file.

DNA DAMAGE

No study on file.

NEUROTOXICITY

Not required at this time.

OTHER

50263-015 182474; Acute oral toxicity; 811; Rat; Northview Pacific Laboratories, Inc Study # X8G081G; 3/15/90; Sodium Bisulfate; 5/sex/dose (except for 3000 mg/kg females: 10 rats), administered by gavage; 1750 (F only), 2000, 2250, 2500, 3000 and 3500 (M only) mg/kg of body weight; mortality: 1750 (F): 1/5; 2000 (M/F): 0/5, 2/5; 2250 (M/F): 1/5; 2500 (M/F): 0/5, 4/5; 3000 (M/F): 3/5, 1/10; 3500 (M): 4/5; clinical signs (dose not specified): weight loss, dehydration, scruffy coats, lethargy and death; necropsy: gross abnormalities observed in the animals that died on test included mottled red lungs and livers mottled with pale areas; several of these animals were also observed to have either lesions on their stomachs or stomachs ruptured with contents emptied into the peritoneal cavity; LD50 (M) = 2800 (2393-3276) mg/kg; the study failed to establish a dose-response for the females; Unacceptable, not upgradeable. (Kellner, 10/1/01).

50263-015 182475; Primary Skin Irritation Study; 815; Rabbit; Northview Pacific Laboratories, Inc., NVP Report # X8G081G; 3/15/90; Sodium Bisulfate; 6 rabbits (sex not specified); A 0.5 g portion of the test material (moistened with deionized water) was applied to two sites, one intact and one abraded, on the back of each animal, applied under two layer thick cotton gauze patches measuring one inch square; the entire trunks of the animals were wrapped in a non-occlusive manner for the twenty-four hours; observations (intact sites): erythema (score 1) was noted in 3/6 rabbits at 24 hours, with clearing by 72 hours; edema (score 1) was seen in 2/6 rabbits at 24 hours and cleared by 72 hours; Toxicity Category IV; Study acceptable. (Kellner, 10/2/01).

Appendix X: UNEP SIDS Sodium Sulfate

FOREWORD **INTRODUCTION**

Sodium sulfate

CAS N°: 7757-82-6

SIDS Initial Assessment Report

For

SIAM 20

Paris, France, 19 – 22 April 2005

1.	**Chemical Name:**	Sodium sulfate
2.	**CAS Number:**	7757-82-6
3.	**Sponsor Country:**	Slovak Republic Contact Point: Centre for Chemical Substances and Preparations, Bratislava Contact Person: Peter Rusnak, Ph.D. Director
	Co-sponsor Country:	Czech Republic Contact Point: Ministry of Environment Contact Person: Karel Bláha, Ph.D. Director Department of Environmental Risks Prague
4.	**Shared Partnership with:**	Sodium Sulfate Producers Association (SSPA)* and TOSOH
5.	**Roles/Responsibilities of the Partners:**	
•	Name of industry sponsor /consortium	Sodium Sulfate Producers Association (SSPA)
•	Process used	Documents were drafted by the consortium, then peer reviewed by sponsor countries experts
6.	**Sponsorship History**	
•	How was the chemical or category brought into the OECD HPV Chemicals Programme?	Nominated by ICCA in the framework of the ICCA HPV program
7.	**Review Process Prior to the SIAM:**	Two drafts were reviewed by the Slovakian/Czech authorities; third draft subject to review by OECD membership
8.	**Quality check process:**	Data was reviewed against the OECD criteria as described in the SIDS manual. These criteria were used to select data for extraction into the SIDS dossier. Original data was sought wherever possible. Originally reported work was deemed reliable if sufficient information was reported (according to the manual) to judge it robust. Reviews were only judged reliable if reported

by reputable organisations/authorities or if partners had been directly involved in their production

9. Date of Submission: Deadline for circulation: 21 January 2005

10. Date of last Update: 13 January 2005

11. Comments:

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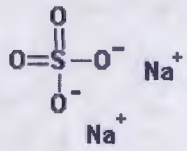
*

The HPV dossier on Sodium sulphate was sponsored by the European Sodium sulphate Producers Association (SSPA). At the time of writing the dossier, members were:	
Adisseo France	FRANCE
Akzo Nobel Nederland NV	THE NETHERLANDS
Alkim Alkali Kimya A.S.	TURKEY
Cordenka	GERMANY
Crimidesa	SPAIN
Elementis Chromium	UNITED KINGDOM
FMC Foret SA	SPAIN
Lenzing AG	AUSTRIA
Minera de Santa Marta	SPAIN
Perstorp AB	SWEDEN
Säteri Oy	FINLAND
Sulquisa	SPAIN
Tessenderlo Chemie SA	BELGIUM
Co Sponsored by:	
TOSOH CORPORATION	Japan

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7757-82-6
Chemical Name	Sodium sulfate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Sulfate (and sodium) ions are important constituents of the mammalian body and of natural foodstuffs and there is a considerable daily turnover of both ions (several grams/day expressed as sodium sulfate). Near-complete absorption of dietary sulfates may occur at low concentration, depending on the counter-ion, but absorption capacity can be saturated at higher artificial dosages resulting in cathartic effects. Absorption through skin can probably be ignored since sodium sulfate is fully ionised in solution. One source suggests that very high levels of sulfate in urine may occur due to absorption from dust inhalation. At dietary levels, excretion is mainly in the urine. Sulfates are found in all body cells, with highest concentrations in connective tissues, bone and cartilage. Sulfates play a role in several important metabolic pathways, including those involved in detoxification processes.

The acute toxicity (LD_{50}) of sodium sulfate has not been reliably established but is probably far in excess of 5000 mg/kg. In an inhalation study with an aerosol, no adverse effects were found at 10 mg/m^3. Also human data indicate a very low acute toxicity of sodium sulfate. Human clinical experience indicates that very high oral doses of sodium sulfate, 300 mg/kg bw up to 20 grams for an adult, are well tolerated, except from (intentionally) causing severe diarrhoea. WHO/FAO did not set an ADI for sodium sulfate. There is no data on acute dermal toxicity, but this is probably of no concern because of total ionisation in solution.

Sodium sulfate is not irritating to the skin and slightly irritating to the eyes. Respiratory irritation has never been reported. Based on wide practical experience with sodium sulfate, in combination with the natural occurrence of sulfate in the body, sensitising effects are highly unlikely.

No suitable dermal and inhalation repeated-dose toxicity studies are available. Valid oral repeated dose toxicity studies with 21, 28 and 35 day studies in hens and pigs are available. Toxicity was confined to changes in bodyweight, water and feed intake and diarrhoea. These changes occurred only at very high doses of sodium sulfate. In ruminants, high concentrations of sulfate in food may result in the formation of toxic amounts of sulfites by bacterial reduction the rumen, leading to poly-encephalomalacia. The available data do not allow the derivation of a NOAEL. Based on available consumer data, a daily dose of around 25 mg/kg/day is well tolerated by humans.

There are no data on *in vitro* and *in vivo* genotoxicity, apart from a negative Ames test. There is no valid oral carcinogenicity study. Limited data from experimental studies support the notion that a substance that is abundantly present in and essential to the body is unlikely to be carcinogenic.

Limited data of poor validity did not provide an indication of toxicity to reproduction.

There are considerable data gaps and the data that are available are not all of standard quality or from animals commonly used for toxicity testing. Nevertheless the weight of evidence, combined with previous assessments of both the sodium ion and sulfic ions lead to the conclusion that the identified data gaps need not necessarily be filled.

Environment

Sodium sulphate is a solid inorganic salt well soluble in water (161-190 g/l at 20 °C) with a melting point of 884 °C and density of 2.7 g/cm³. In water solutions it is fully dissociated to sodium and sulfate ions.

In water sodium sulfate completely dissociates into sodium and sulfate ions. The ions cannot hydrolyse. In anaerobic environments sulfate is biologically reduced to (hydrogen) sulphide by sulfate reducing bacteria, or incorporated into living organisms as source of sulphur, and thereby included in the sulphur cycle. Sodium sulfate is not reactive in aqueous solution at room temperature. Sodium sulfate will completely dissolve, ionise and distribute across the entire planetary "aquasphere". Some sulfates may eventually be deposited, the majority of sulfates participate in the sulphur cycle in which natural and industrial sodium sulfate are not distinguishable

The BCF of sodium sulfate is very low and therefore significant bioconcentration is not expected. Sodium and sulfate ions are essential to all living organisms and their intracellular and extracellular concentrations are actively regulated. However some plants (e.g. corn and *Kochia Scoparia*), are capable of accumulating sulfate to concentrations that are potentially toxic to ruminants.

Algae were shown to be the most sensitive to sodium sulfate; EC_{50} 120h = 1,900 mg/l. For invertebrates *(Daphnia magna)* the EC_{50} 48h = 4,580 mg/l and fish appeared to be the least sensitive with a LC_{50} 96h = 7,960 mg/l for *Pimephales promelas*. Activated sludge showed a very low sensitivity to sodium sulfate. There was no effect up to 8 g/l. Sodium sulfate is not very toxic to terrestrial plants. *Picea banksiana* was the most sensitive species, an effect was seen at 1.4 g/l. Sediment dwelling organisms were not very sensitive either, with an LC_{50} 96h = 660 mg/l for *Trycorythus sp.* Overall it can be concluded that sodium sulfate has no acute adverse effect on aquatic and sediment dwelling organisms. Toxicity to terrestrial plants is also low.

No data were found for long term toxicity. The acute studies all show a toxicity of sodium sulfate higher than 100 mg/l, no bioaccumulation is expected, therefore it can be considered that no further chronic studies are required.

Exposure

Production: production of sodium sulfate is 4.6 million tonnes/year (1999), of which approximately 50% a by-product of the chemical industry and the remainder is extracted from natural deposits.
Use: The main uses are manufacturing of glass and detergents. Other users are from a wide range of industries, including dyeing technology, electrochemical metal treatment, (animal) feeds, pharmaceuticals, textile, semi-conductors, intermediates, agriculture.
Release: Releases to water come from natural sources as well as from detergents and nearly all industrial sources listed above.
Occupational exposure: Exposure to sodium sulfate-containing dusts or aerosols is possible
Consumer products: Exposure to sodium sulfate occurs via drinking water and through naturally occurring or added amounts in foodstuffs. The maximum acceptable concentration for drinking water is 200 – 500 mg/l sulfate, and is based on taste rather than toxicity.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

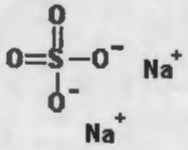
The chemical is of low priority for further work due to its low hazard profile.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 7757-82-6
IUPAC Name: Sodium sulfate
Molecular Formula: Na_2SO_4
Structural Formula:



Molecular Weight: 142.04
Synonyms: Sulfuric acid , disodium salt
Sodium sulfate anhydrous

Sodium sulfate may also occur in hydrated form, usually the hepta- or decahydrate (Glauber's salt)

1.2 Purity/Impurities/Additives

Purity: above 99.5 %. The nature and amounts of impurities are dependent on the production process used., which are quite numerous and may include recycling of waste sulfuric acid from a multiude of industrial processes. Therefore the impurities cannot be specified.

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Reference	Comment
Physical state	Solid		
Melting point	884 °C	Ullmann, 1979 and Handbook of chemistry and Physics, 1997/1998	
Boiling point	Decomposition occurs above 884°C.	Ullmann, 2004	
Density	2.7 g/cm^3 at 20 °C 2.7 g/cm^3 at 25 °C	Ullmann, 1979 Chemiekaarten, 2000	
Vapour pressure	No data		expected to be extremely low
Water solubility	161 g/l at 20 °C 430 g/l at 100 °C	Handbook of chemistry and Physics, 1997/1998 Chapmann & Hall, 1992	
Partition coefficient n-octanol/water (log value)	-3	Chemiekaarten, 2000	
Henry's law constant	No data		The substance is an inorganic salt and it will dissociate in water, therefore it is not of importance.

Sodium sulfate occurs in nature as mineral salts (e.g. thenardite also known as salt cake, and mirabilite also known as Glauber's salt) and is present in almost all fresh and salt waters. Sodium sulfate exists as white crystals or powder, is odourless and has a bitter saline taste.

1.4 Category Justification

A category is not proposed[1]

[1] Although most of the data presented in this monograph are probably applicable to sulfate ions in general, 4 irrespective of the source, care should be taken in extrapolating to other substances. The physico-chemical properties and the toxicity of other sulphate containing compounds will to a large extent be dependent on the counter-ion (e.g. metals other than sodium or organic compounds) and should be assessed separately.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Estimated world-wide production of sodium sulfate was 4.6 million tons in 1999 (U.S. Geological Survey, 2000). The production in the USA is approximately 20% of the world production and in Western Europe this amounts to 35 %. The total production is for approximately 50% a by-product of the chemical industry and the remainder is being extracted from natural deposits.

The main users of sodium sulfate are manufacturers of glass and detergents. Tonnages of sodium sulfate going to detergents (SSPA, 2003) are as follows:
- World total, 1,058,000 Tons,
- Europe, 652,000 Tons (ca. 62 % of world).

These data are valid only for SSPA members. It is difficult to acquire data on glass production and from producers that are not a member of the CEFIC Sodium Sulfate Production Association.

The average concentration of sodium sulfate in detergents (SSPA, 2003) based on a representative sample of 50 commercial detergents, powders and tablets collected in 10 different EU countries (including Eastern) was 20.8 % with a range of 0.0 % to 56.7 %.

Other users are from a wide range of industries, including dyeing technology, electrochemical metal treatment, (animal) feeds, pharmaceuticals, textile, semi-conductors, intermediates, agriculture.

2.2. Environmental Exposure and Fate.

In anaerobic environments sulfate is biologically reduced to (hydrogen)sulfide by sulfate reducing bacteria, or incorporated into living organisms as source of sulfur. Sodium sulfate is not reactive in aqueous solution at room temperature. In moist air sodium sulfate will take up water (hygroscopic) to form hydrates. Sodium sulfate is also soluble in glycerol, but insoluble in alcohol. Sodium sulfate has no oxidising properties, is not explosive and is non-flammable.

2.2.1. Sources of Environmental Exposure

Mineral deposits of sodium sulfate occur naturally around the world. The deposit results from evaporation of inland seas and terminal lakes. Sulfate is a major anion in natural fresh and salt waters and drinking water. The occurrence is mainly due to natural causes, but also to use of sodium sulfate in washing detergents, discharge of industry, mining activities and runoff from fertilized agricultural lands.

Sulfate (sulfur) is an essential nutrient for plants and concentrations of at least 0.5 mg/l in irrigation water are required to prevent detrimental effects on growth.

2.2.2. Photodegradation

There are no data available because no photodegradation can be reasonably expected, based on the character of the substance.

2.2.3. Stability in Water

In water sodium sulfate completely dissociates into sodium and sulfate ions. The ions cannot hydrolyze

2.2.4. Transport between Environmental Compartments

There are no data available on transport between environmental compartments. However, it can be estimated that due to low vapour pressure there is no transfer to or via the atmosphere and that given the very low log Kow (-3 (Chemiekaarten, 2000) and -4.38 (EPI-Suite, 2000)), sodium sulfate is not expected to sorb to sewage sludge or sediments. Some sodium sulfate may be expected in soil due to agricultural use and via irrigation water from rivers.

2.2.5. Biodegradation

Sodium sulfate may be used as an electron acceptor in anaerobic sulfate reduction by sulfate reducing bacteria. Sulfate is converted to (hydrogen)sulfide (Greben, *et al.,* 2000 and Henry *et al.,* 2000).

In the presence of organic substances sodium sulfate is reduced as described in the following reactions:

Sugar: $C_{12}H_{22}O_{11} + 5\ H_2O + 4\ SO_4^{2-} \rightarrow 4\ CO_2 + 8\ H_2 + 4\ HS^- + 8\ HCO_3^- + 4\ H^+$

$8\ H_2 + 2\ SO_4^{2-} + 2\ H^+ \rightarrow 2\ HS^- + 8\ H_2O$

$C_{12}H_{22}O_{11} + 8\ H_2SO_4 \rightarrow 8\ S + 12\ H_2CO_3 + 7\ H_2O$

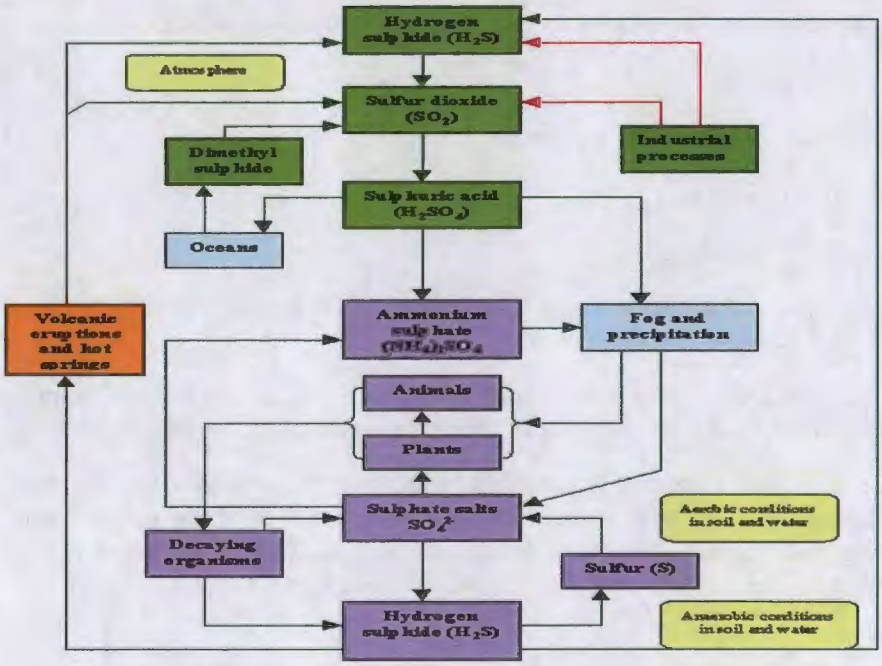
Ethanol: $2\ C_2H_5OH + 3\ SO_4^{2-} \rightarrow 3\ HS^- + 3\ HCO_3^- + 3\ H_2O + CO_2$

$C_2H_5OH + H_2SO_4 \rightarrow 2\ S + 2\ H_2CO_3 + 3\ H_2O$

The sulfur cycle (College of Biological sciences, 2003):

- Assimilative sulfate reduction: sulfate (SO_4^{2-}) is reduced to organic sulfhydryl groups (R-SH) by plants, fungi and various prokaryotes.
- Desulfuration: organic molecules containing sulfur can be desulfurated, producing hydrogen sulfide gas (H_2S).
- Oxidation of hydrogen sulfide produces elemental sulfur (S^o). This reaction is done by the photosynthetic green and purple sulfur bacteria and some chemolithotrophs.
- Further oxidation of elemental sulfur by sulfur oxidizers produces sulfate.
- Dissimilative sulfur reduction: elemental sulfur can be reduced to hydrogen sulfide.
- Dissimilative sulfate reduction: sulfate reducers generate hydrogen sulfide from sulfate.

A schematic representation of the sulfur cycle (http://www.lenntech.com/sulfur-cycle.htm):



2.2.6. Bioaccumulation

Bioconcentration of sodium sulfate was predicted using the EPI-Suite program (2000). The predicted BCF is 0.5, which is very low and does not suggest any concern with respect to bioaccumulation. Sodium and sulfate ions are essential to all living organisms and their intracellular and extracellular concentrations are actively regulated. Some plants (e.g. corn and *Kochia Scoparia*), are capable of accumulating sulfate to concentrations that are potentially toxic to ruminants. (Gould, 1991)

2.2.7. Other Information on Environmental Fate

The following sulfate concentrations in rivers were found on an internet page of United States Environment Program (2001). In the last 100 years sulfate concentrations have greatly increased in some North American rivers because of increased industrial and agricultural activities. In the Volga river the concentration has increased as well due to human activities, from 50 mg/L (natural background) to 60 mg/L since the 1950's. In the Ob river basin of Siberia no significant changes could be observed. The sulfate ion concentration is highly variable in surface waters where it is linked to sulfur-bearing minerals. Sulfate concentrations range from 2 to 30 mg/l for most rivers and lakes in British Columbia. However, some lakes in the Cariboo region and in Richter pass near Osoyoos have particularly high natural sulfate levels of the thousands of mg/l (Ministry of water, land and air protection, British Columbia, Canada, 2000). Most freshwaters contain at least a few parts per million of sulfate, but 20 to 50 ppm or more are common in the eastern United States and most of Europe. Seawater contains levels of about 2700 ppm (Hitchcock, 1975).

Sea salt aerosols are produced in large quantities but do not appear to be a significant source of atmospheric sulfate, except near the place where they are produced due to the fact that they are too

large to remain in the air. Hitchcock (1975) also states that levels of sulfate in air samples in plumes from fossil fuel power-generating plants decline very rapidly with distance from the source even when atmospheric conditions produce minimal dispersion of the plume.

The author measured the following concentrations in the air in North-east America:

- Non-urban sites: 4.9-8.6 $\mu g/m^3$
- Coastal urban sites in New York: 8.1-11.3 $\mu g/m^3$
- Other coastal sites: 10.7-12.2 $\mu g/m^3$
- Inland New York cities: 6.0-10.3 $\mu g/m^3$

Urbanisation does not appear to influence the sulfate levels in North-east America. Most of the sulfate observed in the non-urban sites appears to be of local origin.

Hydrogen sulfide derived from the energy metabolism of bacterial sulfate reducers is the principal source of the 100 to 200 million ton of sulfur annually contributed to the global atmosphere.

Since sodium sulfate is soluble in water it is expected to infiltrate the soil. Most of the ions will migrate downwards through the soil with the penetrating water, for it does not interact with soil given the very low log K_{ow}. Sodium sulfate may run off with surface water when the soil is saturated with moisture e.g. after a rainfall (Environment Canada, 1985).

2.3. Human Exposure

2.3.1. Occupational Exposure

Sodium sulfate can exist as dust (by-product) during manufacturing of various chemicals. Occupational exposure to sodium sulfate is likely by dermal contact and inhalation of the dust

The occupational exposure limit value (OEL) is determined at 10 mg/m^3 (UK) for an 8 hour exposure

2.3.2.Consumer Exposure

Exposure to sodium sulfate occurs via drinking water and through naturally occurring amounts in foodstuffs. In drinking water (wells) concentrations up to 2 g/l were measured in the USA. The taste threshold for sodium sulfate is 250 – 900 mg/l. The maximum acceptable concentration for drinking water is 200 – 500 mg/l sulfate, and is based on taste (Ministry of Environment, Lands and Parks Province of British Columbia, Canada, 2000).

No data on the sulfate content of foodstuffs were found; however, according to WHO, sulfates are used as additives in the food industry and the estimated average daily intake of sulfate in food in the USA is 453 mg/person, based on data on food consumption and reported usage of sulfates as additives (WHO, 2003). An Acceptable Daily Intake for sodium sulfate has not been established.

Potential exposure to consumers also occurs from the use of detergents.

WHO/FAO did not set an ADI for sodium sulfate, since they consider this to be a substance of no concern. This was re-confirmed in the joint WHO/FAO meeting of June 2001.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Sulfate is a normal constituent of the blood and is a normal metabolite of sulfur-containing amino acids, and excess sulfate is excreted in the urine. Daily sulfate excretion is reported to be 0.20 to 0.25 mmol/kg bw/day and higher in children (Health Canada, 1994).

In humans, absorption of small amounts of sulfate from the gut occurs rapidly and almost completely. In a study with 8 volunteers, small amounts (60-80 μCi) of radioactive sulfate-35 (^{35}S) were administered orally or intravenously. Plasma equilibrium was reached within 60 to 105 and 60 to 90 minutes respectively, and in both cases 80% or more of the administered amount of radioactivity was recovered in the urine within 24 hours (Bauer *et al,* 1976). In contrast, absorption studies with very large amounts of sodium sulfate (18.1 gram as decahydrate = 8 g as Na2SO4) demonstrated incomplete absorption (53% urinary recovery of sulfate in 72 hours), which was associated with severe diarrhea (Cocchetto and Levy , 1981). When the same amount was given in four fractions over several hours, urinary recovery was 62% in 72 hours and no or only mild diarrhea occurred. Similar results were obtained with magnesium sulfate, although absorption seems to be less complete and more erratic, thus leading to more adverse effects (Morris and Levy, 1983). Apparently, the capacity of intestinal transport mechanism for sulfates can be exceeded. In a human volunteer study described 3.1.2 (Heizer 1999) , 40-80% of a single dose of 63 mg/kg of sodium sulfate was resorbed and excreted in urine. Effects of saturation of absorption could not be detected over a dose range of 21-63 mg/kg/day in the range-finding part of this study.

After absorption free sulfate ions rapidly distribute over the extracellular space, the apparent volume of distribution being ~ 20% of the body volume. The serum concentration of sulfate in humans ranges between 1.4 and 4.8 mg/100 mL, with a mean of about 3.1 mg/100 mL. Excretion is mainly in urine. The renal clearance is approximately one third of the glomerular filtration rate, indication tubular re-absorption. However, the total free sulfate excretion rate is not dependent on urine flow rate. Organically bound sulfate may follow different excretion patterns. (Cocchetto and Levi, 1981).

About 800 mg of elemental sulfur are eliminated daily through the urine of humans, compared with 140 mg in the faeces. (ICRP, 1984) Some 85% of urinary sulfur is present as inorganic sulfates and a further 10% as organic sulfates, whereas the remainder is excreted as conjugated alkyl sulfates (Diem, 1972).

Similar data are available from experimental animals: In a study on male wistar rats using ^{35}S labeled Na2SO4, rapid and almost complete absorption occurred. When the radioactively labeled material was added to a large amount of unlabeled sodium sulfate and subsequently orally administered, the plasma peak occurred at the same time, but the amount of radioactivity decreased as the dose of unlabeled sulfate increased. This indicates that there is a saturation of the absorption mechanism (Krijgsheld, 1979). In male adult Wistar rats, approximately 73% of dietary calcium or magnesium sulfate salts was absorbed, although absorption was partly dependent on other dietary elements (Health Canada, 1994).

Since disturbances in sulfate metabolism are possibly associated with only one rare form of inherited dwarfism, this area is largely unexplored. Therefore, no attempts have been made to fully describe sulfate metabolism. Sulfate incorporation has been observed with such biologically important compounds as chondroitin, fibrinogen, l-tyrosine derivatives, bilirubin, and steroids. A

number of amino acids contain sulfur and take part in the sulfate cycle. Hydrolytic (sulfatase) activity has been demonstrated in liver, kidney, pancreas, serum, and urine. Sulfates play an important role in sulfoconjugation processes, which are of great importance in a variety of detoxification/excretion processes (Percy, 1964).

In ruminants, excess amounts of sodium sulfate in feed may result in considerable toxicity due to formation of sulfides through bacterial action in the rumen (see section 3.1.5.)

Conclusion: relatively large amounts of sodium sulpfate are normally taken up by the gut from food and drinking water through a saturatable mechanism. Absorbed sodium and sulfate ions circulate freely throughout the entire body and form part of a large intra- and extracellular sodiun and sulfate pool respectively. Sulfates are normally incorporated in a great variety of body compounds and as such essential to life.

3.1.2 Acute Toxicity

The acute toxicity studies conducted with sodium sulfate that could be checked are summarised in the following tables.

Studies in Animals

Oral

Table 2 Acute oral toxicity studies with sodium sulfate

Ref. (year)	Species, strain	Protocol	Administration	Endpoint	Value (mg/kg)
Okahara, (1963)	Mouse	non-standard	oral (?)	LD_{50}	5989 mg/kg bw
Henkel, unpublished	rat	unknown	Oral	LD_{50}	> 10.000 mg/kg bw

Only one LD50 value appears to have been reported in the open literature (in Japanese) (Okahara, 1963). A summary report from Henkel (Henkel, unpublished) stated oral administration of 2-5 ml of a solution in water (concentration not given) to 10 rats (mean body weight 270 gram), with an observation period of 8 days. No symptoms were observed and the LD50 was given as > 10 g/kg. Other data quoted in previous editions of IUCLID could not be found.

Dermal

No valid data are available on the acute dermal toxicity for sodium sulfate. Given the complete dissociation in solution, penetration through the intact skin is not to be expected.

Inhalation

Table 3 Acute inhalation toxicity studies with animals exposed to sodium sulfate

Ref. (year)	Species (strain)	Protocol	Source of mists	Exposure Time	Particle size (MMAD, µm)	Endpoint
Last *et al.* (1980)	Rat (Sprague –Dawley)	non-standard protocol	particle aerosol	72 h	1.15	LOEC> 10 mg/m^3

No standard inhalation studies with Na2SO4 are available. There is one study (Last *et al*, 1980) in which rats were exposed to 10 mg/m3 of Na_2SO_4 as a dry particle aerosol in air with 50% humidity (particle size 1.15 µm Mean Mass Aerodynamic Diameter;, σ_g = 2.5) for 72 hours. These six male rats served as negative controls for rats exposed to various concentrations of sodium sulfite and sodium hydroxymethane sulfonate. Clinical effects were not reported. Compared to the filtered-air control group, no significant changes in various inflammation-related lung tissue parameters, determined post-mortem, were found (DNA, RNA, protein, wet-to-dry weight ratio, glycoprotein secretion in trachea explants).

In a study discussed in more detail in section 3.1.4, effects on serum liver cholinesterase concentration, blood coagulation time, brain irritability and spermatogenesis were claimed after 8 hours exposure to 60 mg/ m^3 Na2SO4 as well as after longer exposures to lower concentrations but these results were considered implausible (Denisov, 1989)

Studies in Humans

Oral

There is one fully controlled study on the effects of sodium sulfate in humans (Heizer 1997). In a range-finding study, four healthy volunteers received controlled amounts of drinking water with stepwise increasing concentrations of sulfate, up to 1200 mg/l of sulfate, over six consecutive two-day periods. The calculated dose of sodium sulfate was 0, 21, 31.5, 42, 52,5 and 63 mg/kg/day. Apart from a faster stool passage, no abnormalities were found. In a subsequent two-day studys en volunteers received of 0 mg on the first and 63 mg sodium sulfate on the second day. A clinically insignificant increase in stool volume, decrease in stool consistency and passage time was noted, but no change in stool frequency or diarrhea.

In another study (US-EPA 1999, Backer L, abstract only) volunteers received bottled water containing 0 to 1200 mg/ l of sulfate for three days and plain water on twos days before and one day after the sulfate exposure. Atually received dose was calculated from returned bottles. There was no effect on bowel movements at any concentration and sulfate dose, although not reported, was stated not be a predictor for diarrhea. . In another abstract of a case-control study (US-EPA,1999, no relationship between sulfate levels and diarrhea was found in infants receiving tap water with sulfate concentrations below 500 mg/l.

Sulfate concentrations above 600 mg/l (equivalent to more than 875 mg/l of sodium sulfate) in well water, used to prepare infant formula was described as a cause of diarrhea without any other sign or symptom of disease in three infants (Chien 1967). The estimated daily dose would have been around 70- 100 mg/kg/day. Although the clinical cause and effect relationship is absolutely clear in these three cases, the number of cases versus the population at risk (i.e. infants with similar oral exposure) is unknown and a dose-effect relationship or threshold concentration cannot be established from three cases. Nevertheless, the author's recommendation not to use water with more than 400 mg of sulfates is in line with WHO standards.

In clinical practice sodium sulfate, alone or with magnesium sulfate, was used as a laxative to induce rapid emptying of the gut, in doses of 300 mg/kg up to 20 grams maximum for an adult. The laxative action is ascribed to fecal fluid retention caused by the hygroscopic action of unresorbed sodium sulfate in the large intestine (Gilman *et al*, 1980). Use of sodium sulfate has been gradually abandoned and the substance has been replaced by other laxatives because of the uncontrollable watery diarrhea and accompanying abdominal cramping it tends to produce.

Other Routes of Exposure

An isotonic (3.89%) solution of sodium sulfate decahydrate, administered intravenously, was used as an antihypercalcemic (Remington, 1980). This practice is considered obsolete.

Conclusion

Only limited data on the acute toxicity of sodium sulfate are available. However, in view of the large body pool of sulfate anions and the high body turnover, the acute toxicity of sulfates must be low, as long as the counter-ion is not toxic. . The laxative effect of oral ingestion is well known and was used medicinally. High dosages given in medical practice with the purpose of inducing diarrhoea were usually accompanied by severe abdominal cramps. Apart from that, no side effects are mentioned in the medical literature."

3.1.3. Irritation

Skin Irritation

Studies in Animals

Table 4 Skin irritation testing with sodium sulfate

Ref. (year)	Species, Test Type	Protocol	Doses	Result
Bayer AG (1991)	Rabbit, Skin irritation test on intact skin	OECD 404, "Acute Dermal Irritation/ Corrosion"	500 mg, Occlusive	Not irritating

Sodium sulfate appears not to be irritating to the skin in rabbit. The study was performed under GLP, and according to international well-accepted guidelines. Endpoint determination was based on the DRAIZE scoring system. The exposure period was 4 hours, under occlusion, and the result was scored after 14 days (Bayer, 1991 unpublished).

Studies in humans

No reports on acute studies in humans are available. Skin problems were not found in a group of 119 workers with long-term exposure to sodium sulfate (see 3.1.4; Kelada & Euinton, 1978)

A human repeated insult skin sensitisation test (see 3.1.4.) was performed with a bath salt allegedly containing 80.8% sodium sulfate on 61 human volunteers, mainly females of all ages. It this test, te test substance was applied under semi-occlusion in a concentration of 1.25%, 8 times for 24 hours and once for 48 hours and induced mild irritation only once in one volunteer.However, the validity of this report could not be assessed (CTFA 1976) Another , unavailable CTFA report (1985) is quoted elsewhere as stating that a 10% solution of sodium sulfate under occlusion for 24 hours produced mild irritation in one out of 19 volunteers.

Eye Irritation

Studies in Animals

Table 5 Eye irritation testing with sodium sulfate

Ref. (year)	Species, Test type	Protocol	Doses	Result
Bayer AG, (1991)	Rabbit, Eye Irritation test	OECD Guideline 405, "Eye Irritation"	90 mg, pulverized	Slightly irritating

Sodium sulfate appears to be slightly irritating to the eye in rabbit. The study was performed under GLP, and according to international well-accepted guidelines. Endpoint determination was based on the DRAIZE scoring system. Sodium sulfate had no adverse effect on the iris and cornea. The substance was instilled into the conjunctival sac of the eye. The positive effects were primarily based on the conjuctivea (redness) observed in the test. The effects were reversible within 7 days. (Bayer, 1991 unpublished).

Conclusion : Sodium sulfate was not a skin irritant in a well conducted study. It is a slight eye irritant with redness of the conjunctiva observed. The redness was reversible within 7 days.

Respiratory Tract Irritation

Studies in Animals

In the acute inhalation toxicity test with 72 hours of exposure described in 3.1.2 (Last *et al*, 1980), no signs of irritation of the respiratory tract were described.

In an experiment set up to determine the difference in inhalatory effects of various sulfur oxide species which occur in ambient air, 5 male rabbits were exposed for one hour to aerosols containing an actual mass concentration of 1800-1950 $\mu g/m^3$ sodium sulfate particles. Mean mass aerodynamic diameter of the aerosol particles was 0.4 µm (σ_g=1.6). Animals served as their own controls through sham exposures. Mucociliary clearance served as an indication of pulmonary irritation. This was determined by means of retention measurements of previously inhaled radioactively labeled microspheres. No effects on mucociliary clearance were found. Since similar exposures with acid sulfates (H2SO4, NH4HSO4) resulted in significant increase in retention time, i.e. lowering of the clearance, whereas (NH4)2SO4 also had no effect, the conclusion is that any irritative effects are not caused by the sulfate ion but by the hydrogen sulfate ion (Schlessinger, 1984)

Studies in humans

An abstract only is available of a study describing the effects of 10 minute inhalation of sodium sulfate aerosols with a mass median aerodynamic diameter of 0.5 µm in concentrations of 2 and 3 3 mg/m^3 on asthmatic and normal adults., with sodium chloride aerosols of the same size as controls. Two out of 5 asthmatics showed an immediate but not dose-dependent drop in FEV_1,but group mean values of respiratory resistance, FEV_1 and VC were comparable up to 60 minutes post-exposure. In a second series, 6 asthmatics and 6 normal adults were followed for 3 hours after 10-minute inhalation of 3 mg/m^3 and no differences were found in the same volume/flow parameters nor in various diffusion capacity parameters (Sackner et al, 1979)

Symptoms indicating local upper respiratory tract irritation were observed in the study by Kelada and Euinton (1978). Workers from natural sodium sulfate mines developed symptoms such as nasal irritation and runny noses (see section 3.1.5).

Conclusion: It is unlikely that short-term inhalation of respirable sodium sulfate particles cause pulmonary irritation.

3.1.4. Sensitisation

Skin and inhalation

Studies in Animals

No valid study was identified for skin sensitisation potential with sodium sulfate.

Studies in Humans

An incomplete report is available on a repeated insult patch test in human volunteers with 10 different cosmetic products, among them bath salt crystals allegedly containing 80.8% sodium sulfate, tested in a concentration of 1.25% under semi-occlusion on 61 human volunteers, mainly females of all ages. The conclusion of the report is that the substance did not demonstrate any potential for inducing allergic sensitization. The validity of this report could not be assessed. (CTFA, 1976)

Sodium sulphate is unlikely to cause allergy, since the body contains large amounts of sulfate (~0.33 mmol/L in serum and about 50 times higher concentration intracellularly) as well as large amounts of sodium ions. Various metal sulfates (e.g. nickel sulfate, cobalt sulfate) are used as standard allergens in routine skin allergy testing, but positive reactions are related to the metal ion, not to the sulfate, as can be deduced from the definitely non-allergenic zinc sulfate (ECETOC, 1999).

Based on the above, it may be concluded that sodium sulfate is not an allergen in humans, and that animal testing for sensitisation potential would not provide any information relevant for hazard identification and risk assessment.

Conclusion

Despite the absence of formal study results, it can be concluded, based on the natural intra- and extracellular occurrence of the substance, that sensitisation to sodium sulfate is highly unlikely

3.1.5. Repeated Dose Toxicity

Studies in Animals

Oral

Validated (reliability 1 or 2) repeated dose toxicity studies with sodium sulfate are summarised in the Table 6. Two reliable non-standard repeated dose toxicity studies were reported. A non-standard. Non-GLP study feeding study in rats was reported and given reliability 2. An invalid carcinogenicity study is reported here since it has (very) limited reliability as a repeated dose study Two veterinary clinical studies are also described which provide valuable clinical observations and could also be given a reliability 2 despite deficiencies with respect to control groups. The reported clinical effects are so severe that they may safely be assumed absent from any control group. Two more studies assigned validity 3 are mentioned in the text but not included in table 6.

Table: 6: Repeated dose toxicity studies with sodium sulfate

Ref. (year)	Species (strain, sex)	Duration, frequency	Administration	Doses	End-point	Value (unit)/ results
Blunck & Crowther (1975)	Rat, Sprague-Dawley, 5 / Male	27 and 44 weeks, daily	In food	0.84 % in diet, 320-400 mg/kg/day	Mortality, tumours , body weight, food and water consumption	NOAEL ~320-400 mg/kg/day
Moinuddinand Wing-Tsit Lee	Rat, 24, male Sprague-Dawley	4 weeks, daily	In food	0.0; ~0.01%ww; Incremental 0.125,0.250, 0.5, 1% 2% (estimated 2000 mg /kg/d)	Food & water consumption, body weight gain, food conversion efficiency, urine production, diarrhoea, blood hemoglobin & white blood count, serum alkaline phosphatase, inorganic phosphate, gross organ pathology	NOAEL 2000 mg/kg/d
Adams *et al.* (1975)	Hen (48 White Leghorn	4 weeks, daily	Drinking water	Concentrations : 250-23328 mg/l Calculated doses per group of 6 hens: 34 mg/kg/d; 45 mg/kg/d 120 mg/kg/d 210 mg/kg/d 550 mg/kg/d 1670 mg/kg/d 4900 mg/kg/d 1650 mg/kg/d	LC_{100}; Body weight, Histopathology, Food and water consumption, Egg production	23328 mg /l at 4,000 mg/l depressed feed consumption and egg production. Increase in water consumption was observed at 4,000 mg/l.

Table: 6: Repeated dose toxicity studies with sodium sulfate (continued)

Ref. (year)	Species (strain, sex)	Duration, frequency	Administration	Doses	End-point	Value (unit)/ results
Veen-huizen *et al.* (1992)	Pig (415, weaned)	28 days, daily	Drinking water	54-1800 mg/l (water consumption/animal & body weights not given)	Body weight, food-water consumption, gastro-intestinal infections	Increased prevalence of diarrhea was a trend as sulfate concentration increased. A non-significant trend in increased water intake was observed with increasing sulfate. No differences in feed intake were observed between various sulfate concentrations. Body weight increased at 600 mg/l and higher.
Gould (1991)	Cattle (9 young steers)	21 days, daily	In food	0.8 % Na-sulfate (0.36% sulfur)	Neurological symptoms, histopathological brain damage, Sulfide formation in rumen	Five out of nine animals developed symptoms and signs of polioencephalomalacia (PEM), onset correlating well with formation of sulfide in rumen
Niles *et al* (2002)	Cattle (15 heifers)	35 days	In food	3860 ppm, 5540 ppm and 7010 ppm of sulfur	Neurological symptoms, histopathological brain damage, Sulfide formation in rumen	All low-dose animals microscopic signs of PEM, all others macroscopic signs of PEM. Onset of symptoms correlated well with formation of sulfide in rumen.

In the study by Blunck and Crowther (1975), also described under Carcinogenicity, two groups of 5 male rats were fed 2% sodium sulfate in the diet for 27 and 44 weeks respectively. No adverse effects were detected with respect to the limited number of endpoints reported from this study. Obviously, group size is too limited to draw firm conclusions bit a tentative NOAEL of >= 320 mg.kg may be deduced. .

In a non-standard non-GLP 4 week repeated dose study comparing the effects of Mg SO_4, Mn SO_4 and Na_2 SO_4, rats were fed an artificial diet enhanced with minimal amounts of MgS04 and MnSO4 but not Na_2SO4; the pure sulfates were added on a mmole/kg food basis. At the top dose, the food contained around 2% of the respective sulfates (calculated to be around 2000 mg/kg/d). While the Mn SO_4 and Mg SO_4-exposed rats showed various functional and even gross pathological aberrations at the top dose, the Na_2SO_4 -exposed rats were comparable to to the controls in every aspect (see table) except slight diarrhoea in one animal for a few days (Moinuddin & Wing-tstit Lee, 1960). Thus the NOAEL from this study is 2000 mg/kg/day

In the studies of Adams et al (1975) and Veenhuizen et al (1992) the test animals were exposed to sodium sulfate in the drinking water which was available on a daily basis. The primary end-points were food and water intake, body weight (occurrence of diarrhoea) and clinical signs of dehydration. In the study (Adams *et al., 1975)* with 48 hens, small and not clearly dose-related effects on food consumption and egg production were observed at concentrations up to and including 4,000 mg/l of sodium sulfate, compared to two weeks of pre-test observations (calculated dose ~ 550 mg/kg/d of sodium sulfate). Water consumption was strongly increased at concentrations of 4000, 5832 mg/l and 16000 mg/l and dramatically decreased at the top level of 23328 mg/l. At 5832 mg/l a serious decline in egg production and decrease of food consumption was observed. At this concentration, the calculated dose was about 1670 mg/kg/d due to increased water consumption. No mortality was observed at 16.000 mg/l (4900 mg/kg/d) but 100 % mortality was observed at 23328 mg/l (only 1644 mg/kg/d due to strongly reduced water consumption) . Necropsy of hens receiving 23340 mg/l sodium sulfate and above showed extreme emaciation and visceral urate deposits. Microscopic examination of kidney tissues showed urate accumulation of individual glomeruli and tubules losing cellular detail in animals receiving 5832 mg/l or more Examinations of other organs were not reported. The above data seem to indicate that the mortality in the top dose was due more to dehydration because of inpalatable drinking water than to the dose of sodium sulfate.

In the study with 415 weaned pigs (Veenhuizen 1992) diarrhoea was observed with increasing test concentrations. No significant effects were observed in feed and water intake at the tested concentrations. Body weight gain was observed at 600 mg/l or higher. Weight gain to feed ratios for all treatments were not different. Isolates of E-coli were found in 14% of the pigs, from 1 pig rotavirus was isolated. No pigs were exposed to transmissible gastroenteritis virus. None of the treatments had an adverse effect on nursery pig performance. During the study one pig died at a concentration of 600 mg/l. Daily doses could not be calculated in the absence of body weigh and water consumption data; percentages only were given.

Another oral study (Upton, 1976) with rats (exposure 6 weeks) indicated that daily dietary supplementation (1-2%) with sodium sulfate did not significantly affect food/water intake and live-weight gain of rats. In an oral chicken study (Sibblad, 1976) effects on weight gain were reported with increasing sodium sulfate in the drinking water (1-5%). The exposure period was 11 days, and no mortality was observed.

In a study with 9 young Holstein steers, a concentrate diet containing 0.8 % sodium sulfate (total sulfur content approximately 0.36%) was given during 21 days. 3 controls were given the same diet without added sodium sulfate (total sulfur or sulfate content not reported). Five out of nine test animals vs. no controls developed clinically manifest poli-encephalomalacia (PEM) as well as

macroscopically visible and histologically recognisable cerebral lesions (brain histology of not-affected animals not reported). The onset of the disease correlated well with increasing concentrations of sulfide in the rumen. Thiamine concentrations in serum (another alleged cause of PEM) were not significantly affected. (Gould *et al.,* 1991)Similar disease due to high sulfur content of food was allegedly also reported earlier in sheep

In another study three groups of young heifers (5 heifers per group) were fed diets with 3860 ppm, 5540 ppm and 7010 ppm of sulfur respectively during 5 weeks. Sulfur concentrations were reached by adding sodium sulfate to the desired level. Microscopic signs of PEM were seen in all four low-dose animals, macroscopic signs in 4/5 medium-dose and 4/5 high-dose animals. Clinical signs of PEM were seen in all animals. Onset of PEM correlated highly with sulfide concentrations in rumen. Other potential causes of PEM were excluded. (Niles *et al*, 2002).

Dermal

No data have been found with respect to repeated dermal toxicity

Combined Inhalation/ oral exposure

An inhalation study on rats was found describing inhalation exposures of 8, 12, 44, 90 and 720 hours duration to $Na_2 SO_4$ concentrations of 60.45, 40.05, 18.03, 11.06 and 3 mg/m3 respectively, with concurrent exposure to sodium sulfate in drinking water at a concentration of 500 mg/l. (estimated dose at the lowest level / longest duration 60 mg/kg/day orally and 1.8 mg/kg/d by inhalation). Small but statistically significant effects were claimed at all concentrations on serum liver cholinesterase concentration (first appearing at 6, 12, 44, 90 and 720 hours respectively), prolongation of blood coagulation time (first appearing at 4, 8, 30, 64 and 510 hours respectively) and brain irritability as measured by "summated threshold potential", (first appearing at 4, 8, 24, 45 and 288 hours respectively), and these effects were stated to be worse at end-of exposure (no data provided). (Denisov *et al*, 1989). Depression of spermatogenesis (presumably at end-of-exposure), was also at all concentrations and all effects were stated to be completely reversible within one month post-exposure (size of recovery groups not given). No abnormalities were observed in number of erythrocytes and leucocytes, total haemoglobin, meth- and sulfhaemoglobin, blood histamine, presence of Heinz-Ehrlich bodies brain cholinesterase, number of sulfhydryl groups, basic phosphatase activity in blood serum and content of ascorbic acid in the adrenals.

However, the documentation of this study is insufficient, some of the results are clearly artificially constructed and incredible and the effects are biologically implausible (see below)

"Similar effects were described in a follow-up 90-day study (Denisov and, Tkachev, 1990) in which rats were exposed to 1 mg/m3 sodium sulfate, or 0.1 and 1 mg/m3 of sodium sulfite or 1 mg/m3 of an unspecified mixture of both, together with 500 mg/l in drinking water, i.e an estimated dose of 60 mg/kg/d orally and 0.6 mg/kg/day by inhalation. Apart from the neuro-physiological and biochemical parameters described above, body weight was also depressed, relative liver weight was decreased, histopathological evidence of serious lung damage and testicular damage was described. Effects were similar for sulfites, sulfates and the mixture, but more severe and earlier for the sulfites. Again, the description of the experiment is insufficient and no actual data are presented. The biological plausibility of such relatively severe effects at such low concentrations, from a compound normally abundantly present in drinking water and food is very much in doubt. There is no reason why a simple, non-reactive and freely circulating ion like sulfate would exert systemic effects when absorbed through the lungs at a fraction of the amount absorbed from the gastro-intestinal tract. These findings also strongly contrast with all other available data.

A possible explanation of the findings from these two studies, if accepted at face value, is contamination of the dust used for the inhalation studies with heavy metals, e.g. cadmium. Spent

sulfuric acid commonly contains heavy metals, so pre-refinery sodium sulfate made from such recycled material may well be contaminated.. In the absence of any analytical data, this cannot be verified.

Studies in Humans

Oral/dermal

No information found.

Inhalation

The effects of long-term inhalation of sodium sulfate dust were determined in a cross-sectional study among 119 male workers from natural sodium sulfate mines (Kelada and Euinton, 1978). Age of the subjects ranged from 17 to 58, exposure duration from two months to 31 years (no control group, study outcomes compared with "normal values", source not given). Dust exposures ranged from less than 5 mg/m3 to 150 mg/m3 during specific tasks (sampling method, strategy, number, frequency and timespan of sampling not given). General medical screening, lung function tests, blood pressure, skin condition, gastro-intestinal functioning, serum sodium, calcium, potassium chloride and sulfate content were all within normal ranges (i.e. presumably as found in the general population). Mean urinary excretion of inorganic sulfate exceeded 2.2 g/liter in all workers and thirty percent of the workers excreted more than 3 g of inorganic sulfate per day, indicating massive uptake from recent exposure. The only subjective symptom indicated by the workers was nasal irritation and runny noses on exposure to dust.

An internal comparison between workers from this group with less than 10 years of exposure (n=77, mean age 28.0 +-10, mean exposure duration 3.1 $\pm$ 2.8 years) with those with more than 10 years exposure (n=42, mean age 45.5 $\pm$ 8.8, mean exposure duration 19.9 $\pm$ 3.6 years) did not show any differences that could not be explained by normal ageing processes There are differences between the group with longer and the group with shorter exposure, but these differences appear to be normal for the respective ages and are therefore attributed to the substantial age difference between groups rather than to exposure to sodium sulfate.No abnormalities were detected that could be explained by exposure to sodium sulfate. (The possibility of a "healthy worker effect" was not addressed in this study).

The study by Denisov and Tkachev (1990) also mentions exposure concentrations in working atmosphere. Shift averages of 88 mg/m3 are given, yet there is no mention of any clinical or biochemical effects on the workers.

Conclusion: A clear NOAEL cannot be derived from the available data. Tentatively a chronic NOAEL of >= 320 mg/kg/day may be deduced from a 27 / 44 week study and a sub-chronic NOAEL of 2000 mg/kg from a 28 day study in rats. Ruminating animals are at risk at much lower levels because of the potential formation of sulfide in the rumen. Since this substance has no discernable systemic toxicity, the tentative chronic NOAEL of >= 320 mg/kg in rats would seem to provide a reasonable margin of safety compared to the estimated daily intake of 453 mg/person/day or around 6.5 to 7.5 mg/kg/day (see 2.3.2)

3.1.6. Mutagenicity

In vitro studies

Table 7 Genetic toxicity in vitro with sodium sulfate

Ref. (year)	Species, Test type	Protocol	Doses	Result
Bayer AG, (1988)	*S. Typhimurium*, Ames test	Salmonella/ Microsome test	312-5000 µg with and without activation	Negative

Sodium sulfate has been shown to be without effect in the Ames test using various strains of *S. typhimurium* (TA1535, TA1537, TA100, TA98) both with and without S9 activation in a GLP standardised test.

In a paper describing cytogenicity studies with sodium bisulfite in human cultured lymphocytes, Meng and Zhang (1992) state that sodium sulfate did not increase the frequencies of chromosomal aberrations, sister chromatid exchanges or micronuclei , nor did it cause changes in mitotic index or cell cycle at concentrations ranging from 5 x 10-5 to 5 x 10-3 M. However, no data are shown and it is not clear from the study description how, when and why these determinations were made. Therefore this study is assigned reliability 4.

Based on the natural intra- and extracellular occurrence of the substance it can be concluded that sodium sulfate is highly unlikely to be mutagenic

3.1.7. Carcinogenicity

Valid standard carcinogenicity studies with sodium sulfate are not available. The carcinogenicity studies listed in Table 8 and described below are those involving the longest exposure to sodium sulfate. Their power to detect any carcinogenic potential that sodium sulfate might possess is extremely low

Table 8 Carcinogenicity studies with sodium sulfate

Ref. (year)	Test Type, Species, Strain	Duration, Frequency	Animal/group	Dose	Result
Blunck & Crowther (1975)	Carcinogenicity, Rat, Sprague-Dawley	27 and 44 weeks, daily	5 / Male	0.84 % in diet, 320-400 mg/kg/day	No mortality, no tumors
Toth (1987)	Carcinogenicity, Swiss albino mice	26 weeks, weekly	50 male, 50 female	31 µg in 0.01 ml sodium chloride (0.9%) per g body weight, s.c. injected	Tumor of subcutis and/or skin in 1% of the female and 4% in male.(normal for this strain in this lab)

In the study of Blunck and Crowther animals were fed an additional 0.84% sodium sulfate in the diet. Because of protocolled food restrictions, the actual additional dose could be calculated and was around 320-400 mg/kg /day. These animals served as controls for animals in which the enhancing effect was studied of the same amount of sodium sulfate on the carcinogenicity of various azo dyes. No carcinogenic effects (tumors) were observed in these control animals. No significant differences in overall body weight gain were observed during the study. Liver weight was not changed. No

evidence of hyperplastic and/or dysplastic change, and no cholangiofibrosis or mild cirrhosis was observed as compared to controls. In addition, no changes in the water or food intake was reported. In the experimental animals fed additional sodium sulfate together with carcinogenic azo dyes, the latency period of tumor development appeared to be reduced, supporting the hypothesis that sulfotransferase plays an important role in the activation of azo dyes.

In a study with mice (Toth, 1987), animals S.C. injected with 31 µg in 0.01 ml of saline per gram body weight (31 mg/kg bw) during 26 weeks served as controls for animals injected with a carcinogenic substance, 4-HMBD. The tumor incidences of the subcutis and skin and of tumors in other organs in the sodium sulfate injected animals were in the normal range observed in the historical untreated control Swiss mice in the same test laboratory.

Conclusion

The limited available data do not allow firm conclusions with respect to carcinogenicity of sodium sulfate. However, they do not contradict the notion that a substance that is abundantly present in and essential to the body, is unlikely to be carcinogenic.

3.1.8. Toxicity for Reproduction

Studies in Animals

Effects on Fertility

One study was found with reliability 4 (Non-standard protocol, non-GLP, insufficient data for assessment, in which 10 female mice per group were exposed to sulfate in the drinking water onwards from one week prior to mating with untreated males. Sodium sulfate concentrations in drinking water were 0 mg/l (distilled water control), 0 mg/l (Na control), .924 mg/l, 1848 mg/l, 3696 mg/l and 7.392 mg/l with sodium concentrations in the Na control and all sodium sulfate groups made identical by addition of $NaHCO_3$ as required.water concentrations correspond to calculated doses of around 140, 280, 560 and 1120 mg/kg/d. Dams with litters from each group were re-bred immediately after weaning. No effects on maternal weight gain, lactational performance, litter size, pup survival and weaning weight at maximum treatment levels over 2 parities were found. However, since it is stated in the paper that only animals with two subsequent litters were involved in the analysis, i.e. ultimately 4 animals/group, and full data on reproductive succes are not given, the effects on fertility cannot be properly assessed. (Andres & Cline, 1989).

The available data on fertility are quite limited but in view of the fact that the substance is abundantly occurring in the body, toxicity for reproduction is unlikely.

Developmental Toxicity

Table 9 Developmental toxicity/teratogenicity studies with sodium sulfate

Ref. (year)	Species, Strain	Protocol	Administration	Exposure time, frequency	Doses	Results
Arcuri & Gautieri (1973)	Mouse, CF-1	Other	SC, single injection	Day 8 or 9 of gestation, single dose	60 mg/kg bw	Increased maternal weight gain, normal litters/ litter size, statistically significant increase in delayed ossifications no other abnormalities,
Seidenberg et al (1986)	Mouse, ICR/SIM	other	gavage	day 8-12	2800 mg/kg bw	no maternal mortality, normal litters/litter size, 100% survival, no visible abnormalities (no necropsy) Increased litter weight on day 1 pn, normal on day 3

Two studies of limited validity were found in the literature. In the study of Arcuri and Gautieri, (1973), which was aimed at documenting teratogenic effects of morhine sulfate, atropine sulfate and physostigmine sulfate, sodium sulfate served as anion control, with sodium chloride as negative control. The study was well documented, with various endpoints (clinical observations, maternal weight ratio, uterine lef/righ horn fetal ratio and resorption ration, fetal weight, sex ratio, skeletal abnormalities, ,soft tissue abnormalities, more specifically exencephaly, cryptorchid test and axial skeletal fusions, but covered only the 8-9 day period of gestation for exposure and the dose of 60 mg/kg was relatively small. There was a statistically significant increase in skeletal abnormalities, described as delayed ossification in the phalanges, sternebrae and skull. Such variations are quite common in tests with rodents and, in the absence of skeletal malformations, generally not regarded as indicative of developmental toxicity. No abnormalities for any of the other end-points were reported.

In another study (Seidenberg *et al.*, 1986) the developmental effects of sodium sulfate in the mouse were examined as part of a validation effort of a developmental screening test. The test substance was administered (2800 mg/kg/day) by gavage on gestation days 8 through 12. No mortality, an unchanged average weight gain, and normal number of litters and neonates/litter were found. A 100 % perinatal survival was found, with an increased postnatal weight at day 1, normal weight at day 3 in the absence of externally visible abnormalities. In a later paper (Seidenberg *et al*, 1987) that summarised the results of this validation test, the outcome of the screening test was considered positive for sodium sulfate, based solely on the increased postnatal weight on day 1 post-partum. However, the significance of such an effect, in the absence of any other effect, is unclear and the reasons for taking this as a positive result are not given

In a summary report (Paterson *et al.*, 1979) the effects of various concentrations of sulfate in drinking water were described on the pregnancy and lactation of sows and gilts (primiparous sows), 58 in total, divided in three groups. Sodium sulfate in drinking water was given in concentrations of 320, 1820 and 3320 mg/l respectively from 30 days post-breeding through 28 days of lactation (body weights and water consumption not given). No effects were found on gestation and lactation in terms of weight gain during gestation, number or weight of piglets at birth or development during lactation. 41 of the newborn piglets, equally representing all treatment groups, were taken from the litters. These newborns were split in three groups and were raised for 28 days on a 18% protein diet plus drinking water containing either 3000 mg/l added sulfate from sodium sulfate, 3000 mg/l

sulfate from magnesium/sodium sulfate or no sulfate added; no differences in development were found between the groups. The study is of not assignable validity.

Studies in Humans

No data.

Conclusion

The limited available data give no indication that sodium sulfate is toxic for reproduction. With regard to the natural occurrence of the substance in the body, developmental toxicity is very unlikely.

3.2 Initial Assessment for Human Health

Sodium sulfate is not known to have acute oral effects other than laxative effects, caused by its hygroscopy. It is not irritating to the skin and is a slight eye irritant. The substance is unlikely to be sensitiser. Oral repeated dose toxicity is limited to diarrhoea and subsequent dehydration at dosages far higher than the normal daily intake from food and water. Ruminant animals may develop serious brain disorders from high sulfate content in food and water due to formation of sulfides in the rumen but this is not relevant to humans. Limited inhalation data from humans do not indicate serious concerns with respect to acute or chronic dust inhalation. There is limited data on reproduction which give not indication that sodium sulfate is toxic for reproduction. There is no valid data on carcinogenicity. However, given the natural occurrence in the body of this substance which is essential to life, carcinogenicity and toxicity for reproduction is not an issue.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute toxicity

Effects in fish

Three studies were reliable with restrictions as the studies were not performed according to standardised guidelines, but were performed using an adequate scientific methodology and described with enough details (see table 10). No studies were performed under GLP. All three tests were performed in reconstituted water. In two tests a concentration range of the test substance and determination of test parameters are described. The study with *Pimephales promelas* was performed according to EPA guideline with determination of test substance concentrations (ion-chromatography). During two studies (with *Lepomis macrochirus*, Trama (1954) and *Pimephales promelas*, Mount *et al.* (1997)) the critical confounding factors pH and oxygen were within acceptable ranges, while in the third study (with *Lepomis macrochirus*, Patrick *et al.* (1968)) these parameters were not indicated. The acute toxicity for fish is very low, with LC_{50} values far above 1,000 mg/l for both species, *Lepomis macrochirus* and *Pimephales promelas*.

Table 10 Validated data (validity 1 or 2) on acute toxicity to fish.

	Ref. (year)	Species	Method/ Protocol	Results
Acute/ prolonged toxicity to fish	Trama (1954)	*Lepomis macrochirus*	Concentration range in reconstituted water	LC_{50} 96h = 13,500 mg/l; LC_0 = 8,700 mg/l.
	Patrick *et al.* (1968)	*Lepomis macrochirus*	96 hours test, based on Cairns *et al.* (1964)	LC_{50} 96h = 13,500 mg/l
	Mount *et al.* (1997)	*Pimephales promelas*	96 hours test, based on EPA/600/4-90/ 027 (1991) guideline.	LC_{50} 96h = 7,960 mg/l

Effects in aquatic invertebrates

Only one reference describing a *Daphnia magna* test in 48 hours (Mount *et al.*, 1997) was assigned validity 2. This test was not performed under GLP, but was performed according to EPA guideline, with determination of test substance (ion-chromatography), and details on test performance and statistics.

As indicated the toxicity of sodium sulfate for *Daphnia* is very low, with an EC_{50} value far above 1000 mg/l.

Table 11 Validated data (validity 2) on acute toxicity to aquatic invertebrates.

	Ref. (year)	Species	Method/Protocol	Results
Acute toxicity to aquatic invertebrates	Mount *et al.* (1997)	*Daphnia magna*	48 hours test, based on EPA/600/4-90/ 027 (1991) guideline.	EC_{50} 48h = 4,580 mg/l; EC_{50} 24 h = 6,290 mg/l.

Effects in aquatic plants / algae

The only valid study was a 120-hour growth test with *Nitzschia linearis* (Patrick *et al.*, 1968). It was classified as valid with restrictions, as a different species was used and a greater test duration than recommended in the OECD-guidelines. An EC_{50} value of 1,900 mg/l was calculated.

Table 12 Validated data (validity 2) on acute toxicity to aquatic plants.

	Ref. (year)	Species	Method/Protocol	Results
Acute toxicity to aquatic plants	Patrick *et al.* (1968)	*Nitzschia linearis*	120 hours test, based on Cairns *et al.* (1964)	EC_{50} 120h = 1,900 mg/l

Effects in sediment dwelling organisms

There are four studies found with sediment dwelling organisms (*Lymnea* and Polychaeta) of which the publications are not available. There was one study found that was considered valid with restrictions. It was an acute semi static test with *Trycorythus sp.* performed in river water (Goetsch and Palmer, 1997). The method used was not a standard method but it was described in detail and considered appropriate. The EC_{50} values for *Lymnea sp.* and *Lymnea sp.* eggs are 799 and 3,553 mg/l respectively. The toxicity for the marine worm *Ophryotrocha labronica* was determined at 5.4 mg/l (Saliba and Ahsanullah, 1973), which deviates enormously from the effects to other

invertebrates. As the original publication(s) are not available, conclusions on the sensitivity of soil dwelling organisms cannot be drawn.

Three studies on mosquito and mosquito larvae (*Culex sp.*) were found (Dowden, 1961; Dowden and Bennet, 1965), two were not available and one was documented insufficiently. The toxicity data of these tests indicate that the toxicity of sodium sulfate for these terrestrial organisms is low (EC_{50} values of > 1000 mg/l for both adults and larvae).

Chronic Toxicity

No data were found in the literature search for long term toxicity.

Toxicity to Microorganisms

Four studies on activated sludge bacteria, motile protozoa and stalked ciliates were reliable with restrictions as the studies were not performed according to standardised guidelines, but were described with enough details. There was no effect on the microorganisms up to approximately 8 g/l (Tokuz & Eckenfelder (1979), Tokuz (1986), Gilli & Comune (1980)). Two studies on the toxicity to *Pseudomonas fluorescens and Pseudomonas putida* were found but were not available.

Table 13 Validated data (validity 1 or 2) on acute toxicity to microorganisms.

	Ref. (year)	Species	Method/Protocol	Results
Acute toxicity to micro-organisms	Tokuz & Eckenfelder (1979), Tokuz (1986)	Bacteria in activated sludge	37 days test with increasing concentration	NOEC ca. 26 g/l
	Tokuz & Eckenfelder (1979), Tokuz (1986)	Motile protozoa in activated sludge	37 days test with increasing concentration	NOEC ca. 26 g/l
	Tokuz & Eckenfelder (1979), Tokuz (1986)	Stalked ciliates in activated sludge	37 days test with increasing concentration	NOEC ca. 8 g/l
	Gilli & Comune (1980)	Activated sludge	ca. 40 days test with increasing concentration	NOEC ca. 30 g/l

With respect to the high NOEC values sodium sulfate is not expected to be hazardous for activated sludge.

4.2 Terrestrial Effects

Effects in soil dwelling biota

There are no data available

Table 14 Validated data (validity 2) on acute toxicity to sediment dwelling organisms.

	Ref. (year)	Species	Method/Protocol	Results
Acute toxicity to sediment dwelling organisms	Goetsch and Palmer (1997)	*Trycorythus sp.*	96 hours semi static test in river water	LC_{50} 96h = 0.66 g/l

Effects in terrestrial plants

There were six studies found on terrestrial plants. Three (Navarro, *et al.*, 2002; Banet, *et al.*, 1996; Egan and Ungar, 1998) were considered invalid because it was not clear at what concentrations significant effects occurred. In two of these studies the test concentration was expressed in osmotic potential and it is not clear what the equivalent sodium sulfate concentration is. Three studies were valid with restrictions. The methods were not standardised, but described in detail. *Pinus banksiana* appeared to be the most sensitive to sodium sulfate and the roots appeared to be the most sensitive part of the plant. Root length and the number of lateral roots were affected at 10 mM (1.4 g/l) (Croser, *et al.*, 2001).

Table 15 Validated data (validity 1 or 2) on toxicity to terrestrial plants

	Ref. (year)	Species	Method/Protocol	Results
Toxicity to terrestrial plants	Croser, *et al.* (2001)	*Picea glauca*	Test with seeds in sand	Emergence: decrease in 20 mM and higher Survival: decrease in 50 mM and higher Root length: reduction in 20 mM and higher Lateral roots: decrease in 50 mM and higher Leaf necrosis: in 50 mM and higher Fresh weight: reduced in 50 mM and higher Photosynthesis: not changed
	Croser, *et al.* (2001)	*Pinus banksiana*	Test with seeds in sand	Emergence: decrease in 20 mM and higher Survival: decrease in 50 mM and higher Root length: reduction in 10 mM and higher Shoot length: reduced in 50 mM and higher Lateral roots: decrease in 10 mM and higher Leaf necrosis: in 50 mM and higher Fresh weight: reduced in 50 mM and higher PHOTOSYNTHESIS: NOT CHANGED
	Croser, *et al.* (2001)	*Picea mariana*	TEST WITH SEEDS IN SAND	Emergence: decrease in 100 mM and higher Survival: decrease in 100 mM and higher Shoot length: reduced in 50 mM and higher Root length: reduction in 20 mM and higher Lateral roots: decrease in 50 mM and higher Leaf necrosis: no necrosis Fresh weight: reduced in 50 mM and higher Photosynthesis: not changed

4.3 Other Environmental Effects

No data on other environmental effects are available.

4.4 Initial Assessment for the Environment

For short term toxicity many studies were performed, but most were not considered reliable. There were no studies with reliability 1, but for every SIDS endpoint at least one study was found which was valid with restrictions. Algae were shown to be the most sensitive to sodium sulfate; EC_{50} 120h = 1,900 mg/l. For invertebrates *(Daphnia magna)* the EC_{50} 48h = 4,580 mg/l and fish appeared to be the least sensitive with a LC_{50} 96h = 7,960 mg/l for *Pimephales promelas*.

Activated sludge showed a very low sensitivity to sodium sulfate. There was no effect on the stalked ciliates in the activated sludge up to 8 g/l, the bacteria and motile protozoa showed no effect up to 26 g/l.

Sodium sulfate is not very toxic to terrestrial plants. *Picea banksiana* was the most sensitive species. The roots appeared to be the most sensitive part of the plant and showed effects at 1.4 g/l. Sediment dwelling organisms were not very sensitive either, with an LC_{50} 96h = 660 mg/l for *Trycorythus sp.*

Overall it can be concluded that sodium sulfate has no acute adverse effect on aquatic and sediment dwelling organisms. For terrestrial plants it is not very toxic either.

Sulfate can be reduced anaerobically by sulfate reducing bacteria to sulfide, but will not be aerobically degraded.

No data were found in the literature search for long term toxicity. The acute studies all show LC50s and EC50s for sodium sulfate that are substantially higher than the EU (European Union, 1967) and GHS (United Nations, 2003) threshold for classification as dangerous for the environment (100 mg/l). The calculated BCF is 0.5, which means that no bioaccumulation is expected. From these results it can be considered that no further chronic studies are required.

5 RECOMMENDATIONS

Because of low toxicity to humans and the environment, the chemical is of low priority for further work.

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I U C L I D

D a t a S e t

Existing Chemical	ID: 7757-82-6
CAS No.	7757-82-6
EINECS Name	sodium sulphate
EC No.	231-820-9
TSCA Name	Sulfuric acid disodium salt
Molecular Formula	H2O4S.2Na
Producer Related Part	
Company:	Akzo Nobel Salt and Basic Chemical Division
Creation date:	06-SEP-2001
Substance Related Part	
Company:	Akzo Nobel Salt and Basic Chemical Division
Creation date:	06-SEP-2001
Memo:	OECD HPV Chemical Programme, SIDS DOssier, approved at SIAM 20 (19-22 April 2005)
Printing date:	07-AUG-2006
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Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 Applicant and Company Information

24-OCT-2001

1.0.2 Location of Production Site, Importer or Formulator

1.0.3 Identity of Recipients

1.0.4 Details on Category/Template

1.1.0 Substance Identification

IUPAC Name: sodium sulfate
Mol. Formula: Na2SO4
Mol. Weight: 142.04
Petrol Class: other

22-JUN-2005

1.1.1 General Substance Information

Purity type: other
Substance type: inorganic
Physical status: solid
Purity: > 99.5

Source: United States Pharmacopeial (2000)
31-OCT-2001

1.1.2 Spectra

1.2 Synonyms and Tradenames

Alcan recovered Cryolite

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Bisodium sulfate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Dibasic sodium sulfate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Dinatriumsulfat

Source: Henkel KGaA Duesseldorf
01-NOV-2001

Disodio monosolfato

Source: Luigi Stoppani SpA Milano
30-OCT-2001

Disodium monosulfate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Disodium sulfate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Disodium sulphate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

E 514

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Kemsol

Source: Henkel KGaA Duesseldorf
01-NOV-2001

Na-sulfat

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Natrii sulfas

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Natrium sulfuricum

Source: SYNTANA Handelsges. Muhlheim-Ruhr
30-OCT-2001

natriumsulfaatti

Source: Sateri Oy Valkeakoski
30-OCT-2001

Natriumsulfat rein

Source: Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
Faserwerk Kelheim GmbH Kelheim
30-OCT-2001

Natriumsulfate wasserfrei

Source: Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
Faserwerk Kelheim GmbH Kelheim
30-OCT-2001

Ningunoso

Source: CRIMIDESA Madrid
01-NOV-2001

Sal disodica del acido sulfurico

Source: FMC FORET SA Barcelona
30-OCT-2001

Salt cake

Source: Courtaulds Fibres Limited Grimsby
Henkel KGaA Duesseldorf
Occidental Chemical Corporation Niagara Falls, NY 14302-0728
30-OCT-2001

saureregualator E 514

Source: Henkel KGaA Duesseldorf
01-NOV-2001

Schwefelsaure, di-Na-Salz

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Schwefelsaure-Natriumsalz

Source: MERCK Darmstadt
30-OCT-2001

Sodium sulfate (anydyrous)

Source: Amway Europe Zaventem
30-OCT-2001

Sodium sulphate anhydrous

Source: Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Solfato di sodio

Source: Laporte Italia SPA Divisione SILO Torino
30-OCT-2001

Sulfate de Sodium

Source: Produits Chimiques de Loos Loos
30-OCT-2001

Sulfato de sodio anidro

Source: Industrias Lever Portugesa LDA. Sacavem; ECB - Existing Chenicals Ispra (VA); Henkel KGgA Dueseldorf
01-NOV-2001

Sulfato sodico

Source: FMC FORET SA Barcelona
01-NOV-2001

Sulfato sodico anhidro

Source: S.A. Sulquisa Bilbao
30-OCT-2001

Sulfuric acid, disodium salt

Source: Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
Novo Nordisk A/S Bagsvaerd
30-OCT-2001

Thenardite

Source: Chemie GmbH Bitterfeld-Wolfen Wolfen
30-OCT-2001

Trona

Source: Chemie GmbH Bitterfeld-Wolfen Wolfen
01-NOV-2001

1.3 Impurities

1.4 Additives

1.5 Total Quantity

Quantity: ca. 4600000 tonnes produced in 1999

22-SEP-2005 (100)

Quantity: ca. 4928000 tonnes produced in 1991

22-SEP-2005 (94)

1.6.1 Labelling

30-OCT-2001

1.6.2 Classification

Classified: no classification required (no dangerous properties)

30-OCT-2001

1.6.3 Packaging

1.7 Use Pattern

Type: industrial
Category: Agricultural industry

30-OCT-2001

Type: industrial
Category: Basic industry: basic chemicals

30-OCT-2001

Type: industrial
Category: Chemical industry: used in synthesis

30-OCT-2001

Type: industrial
Category: Metal extraction, refining and processing of metals

30-OCT-2001

Type: industrial
Category: Paints, lacquers and varnishes industry

30-OCT-2001

Type: industrial
Category: Paper, pulp and board industry

30-OCT-2001

Type: industrial
Category: Personal and domestic use

30-OCT-2001

Type: industrial
Category: Public domain

30-OCT-2001

Type: industrial
Category: Textile processing industry

30-OCT-2001

Type: industrial
Category: other: Detergent industry

30-OCT-2001

Type: industrial
Category: other: Glassindustry

30-OCT-2001

Type: use
Category: Cleaning/washing agents and disinfectants

30-OCT-2001

Type: use
Category: Conductive agents

30-OCT-2001

Type: use
Category: Fillers

30-OCT-2001

Type: use
Category: Food/foodstuff additives

30-OCT-2001

Type: use
Category: Intermediates

30-OCT-2001

Type: use
Category: Laboratory chemicals

30-OCT-2001

Type: use
Category: Pesticides

30-OCT-2001

Type: use
Category: Pharmaceuticals

30-OCT-2001

Type: use
Category: Process regulators

30-OCT-2001

Type: use
Category: Semiconductors

30-OCT-2001

1.7.1 Detailed Use Pattern

1.7.2 Methods of Manufacture

1.8 Regulatory Measures

01-NOV-2001

1.8.1 Occupational Exposure Limit Values

Type of limit: MAC (NL)

Remark: not determined
Reliability: (4) not assignable
no data available
22-SEP-2005 (24)

Type of limit: OES (UK)

Remark: O.E.L. : 10 mg/m3 8hr. TWA total inhalable dust.
O.E.L. : 5 mg/m3 8hr. TWA total respirable dust.
Reliability: (4) not assignable
Original reference not available
22-SEP-2005 (75)

1.8.2 Acceptable Residues Levels

1.8.3 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 0 (generally not water polluting)

22-SEP-2005 (19)

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 0 (generally not water polluting)

22-SEP-2005 (2)

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 0 (generally not water polluting)

19-JUN-2003 (18)

1.8.4 Major Accident Hazards

1.8.5 Air Pollution

1.8.6 Listings e.g. Chemical Inventories

1.9.1 Degradation/Transformation Products

1.9.2 Components

1.10 Source of Exposure

Source of exposure: Human: exposure by production
Exposure to the: Substance

Remark: Sodium sulfate in solution is a by product from the manufacture of Sodium Dichromate.
The solution, after separation of the minimal Sodium Dichromate content, is evaporated to saturation.The resultant crystals of Sodium sulfate are separated from solution by centrifuge prior to drying.
22-SEP-2005 (17)

1.11 Additional Remarks

Memo: Clinical use as laxative

Remark: Sodium sulfate, recommended dose:
300 mg/kg up to 20 grams maximum for an adult.
Probable mode of action: fluid retention caused by the hygroscopic action of unresorbed sodium sulfate in the large intestine.
Reliability: (4) not assignable
textbook reference
13-JAN-2005 (41)

Memo: Drinking Water Quality Standards

Remark: Sulfate Maximum Acceptable Concentration: 200 mg/l
Sulfate Maximum Allowable Concentration : 250 mg/l
01-NOV-2001 (74)

Memo: Drinking Water Quality Standards

Remark: The taste threshold concentrations for sodium sulfate is 250 - 900 mg/l.
16-NOV-2001 (3)

Memo: Drinking Water Quality for Poultry

Remark: Sulfate : Level considered average : 125 mg/l
Sulfate : MAC : 250 mg/l
22-JUN-2005 (88)

Memo: Ground water Quality Standards for Drinking water purposes

Remark: Sulphate Maximum Acceptable Concentration: 200 mg/l
Sulphate Maximum Allowable Concentration : 250 mg/l
01-NOV-2001 (74)

Memo: Secondary Maximum Contaminant Level

Remark: SMCL value : 250 mg/l Sulfate
01-NOV-2001 (76)

Memo: Speciation of urinary sulfur

Remark: 85% of urinary sulfur as s inorganic sulfates
10% as organic sulfates,
5% as conjugated alkyl sulfates
Reliability: (4) not assignable

textbook reference
13-JAN-2005 (31)

Memo: Sulfate elimination

Remark: Daily elimination of sulfate in human urine: ~ 800 mg as elemental sulfur are
Daily elimination of sulfate in human feces: : ~ 140 mg
Reliability: (4) not assignable
textbook reference
13-JAN-2005 (57)

Memo: Water Quality Guidelines for Sulfate

Remark: Drinking water (Aesthetics) : 500 mg/l dissolved sulfate
Freshwater Aquatic Life : 100 mg/l sulfate maximum concentration, 50 mg/l sulfate Alert level.
22-JUN-2005 (3)

1.12 Last Literature Search

1.13 Reviews

2.1 Melting Point

Value: = 800 degree C

Reliability: (2) valid with restrictions
Results from handbook
01-NOV-2001 (67)

Value: = 884 degree C

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available.
However, there is no need to perform such studies because:
- Exisiting data are available from at least 3 different sources from which the results are not conflicting.
07-NOV-2001 (101)

Value: ca. 884 degree C

Reliability: (2) valid with restrictions
Results from handbook
Flag: Critical study for SIDS endpoint
31-OCT-2001 (47)

Value: ca. 888 degree C

Reliability: (2) valid with restrictions
Results from handbook
07-NOV-2001 (49)

2.2 Boiling Point

Value:
Decomposition: yes

Test substance: as prescribed by 1.1 - 1.4

Result: Decomposes at temperatures above melting point (884 degree C).
Reliability: (2) valid with restrictions
Results from handbook
Flag: Critical study for SIDS endpoint
01-DEC-2004 (102)

Value: ca. 103.5 degree C

Remark: Determined in a saturated solution
Reliability: (2) valid with restrictions
Results from handbook
16-NOV-2001 (63)

Value: > 1700 degree C

Reliability: (2) valid with restrictions
Results from handbook
31-OCT-2001 (24)

2.3 Density

Type: relative density
Value: = 2.7 g/cm³ at 20 degree C

Reliability: (2) valid with restrictions
Results from handbook
Flag: Critical study for SIDS endpoint
13-JUN-2003 (101)

Type: relative density
Value: = 2.7 g/cm³ at 25 degree C

Reliability: (2) valid with restrictions
Results from handbook
13-JUN-2003 (24)

Type: relative density
Value: = 2.671 g/cm³

Reliability: (2) valid with restrictions
Results from handbook
13-JUN-2003 (49)

Type: relative density
Value: ca. 2.7 g/cm³

Reliability: (2) valid with restrictions
Results from handbook
31-OCT-2001 (47)

2.3.1 Granulometry

2.4 Vapour Pressure

Remark: The melting point is 800-888 degree C. therefore, the vapour pressure will be extremely low.
13-JUN-2003

2.5 Partition Coefficient

Partition Coeff.: octanol-water
log Pow: = -4.38

Method: other (calculated)

Reliability: (2) valid with restrictions

Result calculated with computer program
01-SEP-2003 (38)

Partition Coeff.: octanol-water
log Pow: = -3

Method: other (calculated)

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
19-JUN-2003 (24)

2.6.1 Solubility in different media

Solubility in: Water
Value: = 190 g/l at 20 degree C

Reliability: (2) valid with restrictions
Results from handbook
31-OCT-2001 (101)

Solubility in: Water
Value: ca. 430 g/l at 100 degree C

Reliability: (2) valid with restrictions
Results from handbook
07-NOV-2001 (23)

Solubility in: Water
Value: ca. 195 g/l at 20 degree C

Reliability: (4) not assignable
Results from handbook
16-JUN-2003 (63)

Solubility in: Water
Value: ca. 162 g/l at 20 degree C

Reliability: (2) valid with restrictions
Results from handbook
07-NOV-2001 (24)

Solubility in: Water
Value: ca. 161 g/l at 20 degree C

Reliability: (2) valid with restrictions
Results from handbook
15-NOV-2004 (47)

Solubility in: other: Glycerol

Remark: Sodium sulfate is soluble in glycerol

Reliability: (4) not assignable
Secondary literature. Reference not available.
16-JUN-2003 (67)

Solubility in: other: Alcohol

Remark: sodium sulfate is not soluble in alcohol
Reliability: (4) not assignable
Secondary literature. Reference not available.
16-JUN-2003 (67)

2.6.2 Surface Tension

2.7 Flash Point

2.8 Auto Flammability

2.9 Flammability

Result: non flammable

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
31-OCT-2001 (24)

2.10 Explosive Properties

Result: not explosive

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
31-OCT-2001 (24)

2.11 Oxidizing Properties

Result: no oxidizing properties

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
23-NOV-2001 (24)

2.12 Dissociation Constant

2.13 Viscosity

Value: = 2.481 mPa s (dynamic) at 20 degree C

Result: 22% solution

Test substance: as prescribed by 1.1 - 1.4

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.

02-DEC-2004 (48)

2.14 Additional Remarks

Memo: Data refer to dehydrated Na2SO4

Source: Enichem S.p.A Milan
Henkel S.p.A Duesseldorf

16-NOV-2001

3.1.1 Photodegradation

3.1.2 Stability in Water

Type: abiotic

Remark: Na2SO4 dissociates in water completely in sodium and sulfate ions. The ions cannot hydrolyze and therefore it is not scientifically necessary to perform a hydrolysis study.
Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
22-SEP-2005 (47)

3.1.3 Stability in Soil

3.2.1 Monitoring Data (Environment)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. 3 - 30 mg/l

Remark: Sulfate concentrations measured in Canadian Lakes, British Columbia, Canada.
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
22-SEP-2005 (58)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. .001 - 3 g/l

Remark: Sulfate concentrations measured in rivers in Western Canada, British Columbia, Canada
Reliability: (4) not assignable
Reference not available
22-SEP-2005 (37)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. 2 - 30 mg/l

Remark: Sulfate concentrations measured in the Liard river, British Columbia, Canada
Reliability: (4) not assignable
Reference not available
22-SEP-2005 (15)

Type of measurement: background concentration
Medium: surface water
Concentration: > .4 - g/l

Remark: Sulfate concentration measured in the Great Plains shales, USA.
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific

principles, acceptable for assessment
22-SEP-2005 (103)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. 10 - mg/l

Remark: Sulfate concentration measured in the Ob River, Siberia, USSR.
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
22-SEP-2005 (103)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. 50 - 60 mg/l

Remark: Sulfate concentrations measured in the Volga river, USSR.
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
22-SEP-2005 (103)

Type of measurement: background concentration
Medium: drinking water
Concentration: ca. .006 - 1.6 g/l

Remark: Sulfate concentrations measured at swine farms in Ohio, USA
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
26-SEP-2005 (107)

Type of measurement: background concentration
Medium: drinking water
Concentration: ca. 1 - 2 g/l

Remark: Sulfate concentrations measured in drinking water wells in North and South Dakota, USA
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
22-SEP-2005 (69)

Medium: air

Result: North America:
· Non urban sites: 4.9-8.6 µg/m3
· Coastal urban sites in New York: 8.1-11.3 µg/m3
· Other coastal sites: 10.7-12.2 µg/m3
· Inland New York cities: 6.0-10.3 µg/m3
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment.
22-SEP-2005 (54)

3.2.2 Field Studies

01-NOV-2001

3.3.1 Transport between Environmental Compartments

3.3.2 Distribution

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic

Remark: It is not possible to have aerobic biodegratation of sulfate.

13-JUN-2003

Type: anaerobic
Inoculum: anaerobic sludge
Result: other: see freetext

Method: other: see freetext
Year: 2000
Test substance: as prescribed by 1.1 - 1.4

Result: Sulfate was reduced according to the following reactions:
- Sugar:
$C_{12}H_{22}O_{11} + 5\ H_2O + 4\ SO_4^{2-} \rightarrow 4\ CO_2 + 8\ H_2 + 4\ HS^- + 8\ HCO_3^- + 4\ H^+$
$8\ H_2 + 2\ SO_4^{2-} + 2\ H^+ \rightarrow 2\ HS^- + 8\ H_2O$
$C_{12}H_{22}O_{11} + 8\ H_2SO_4 \rightarrow 8\ S + 12\ H_2CO_3 + 7\ H_2O$
- Ethanol:
$2\ C_2H_5OH + 3\ SO_4^{2-} \rightarrow 3\ HS^- + 3\ HCO_3^- + 3\ H_2O + CO_2$
$C_2H_5OH + H_2SO_4 \rightarrow 2\ S + 2\ H_2CO_3 + 3\ H_2O$

Test condition: - Inoculum: Anaerobic sludge obtained from the local municipal sewage treatment plant.
- Concentrations of test chemicals: $CaSO_4$ and COD (sugar and technical ethanol) both 1500 mg/l
- Temperature: 21 degree C
- Analytical determinations: All concentrations, alkalinity and pH were measured according to standard analytical procedures (APHA, 1985).

Reliability: (2) valid with restrictions
No guideline study, but includes detailed information on used method and endpoints.

22-SEP-2005 (46)

Type: anaerobic

Remark: Na_2SO_4 may be used as an electron acceptor in anaerobic sulfate reduction by sulfate reducing bacteria. Sulfate is converted to (hydrogen)sulfide.

Reliability: (3) invalid
Test is not applicable, but it gives some results about sulfate reduction.

22-SEP-2005 (53)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

BCF: = .5

Method: other: calculated

Remark: This result is calculated on the basis of log Kow = -2.20 from Sulfuric acid, because it cannot be calculated for Sodium. It is not expected that the value will be different for Sodium sulfate.

Reliability: (2) valid with restrictions
Result calculated with computer program

22-SEP-2005 (38)

3.8 Additional Remarks

Memo: BIOGENIC CONTRIBUTION

Remark: Study on the biogenic contribution to atmospheric levels of sulfate. study performed in the USA.
Results:
Hydrogen sulfide derived from the energy metabolism of bacterial sulfate reducers is the principal source of the 100 to 200 million ton of sulfur annually contributed to the global atmosphere.
Most of the sulfate observed in the nonurban sites appears to be of local origin in the north-east of the USA.
Urbanization does not appear to influence the sulfate levels in the north-east of the USA.

Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment

22-JUN-2005 (54)

Memo: PLANT NUTRIENTS

Remark: Sulfate concentrations of less than 0.5 mg/l in water is detrimental for plant growth, as sulfur is an essential element in living organisms.

Reliability: (4) not assignable
Reference not available

11-JUL-2003 (3)

4.1 Acute/Prolonged Toxicity to Fish

Type:	static
Species:	Lepomis macrochirus (Fish, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: no
LC50:	= 12500 - 13000
Limit Test:	no
Method:	other: see freetext, method based on Doudoroff et al (1951). Bio-assays methods for the evaluation of acute toxicity of industrial wastes to fish. Sewage and Industrial Wastes, 23, (11):1380-1397.
Year:	1959
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED: Doudoroff et al (1951). Tests performed in standardized test medium. Test parameters pH, oxygen and temperature not reported. Concentration ranges not known. Study performed to evaluate differences between three size ranges of fish. STATISTICAL METHODS: not described. METHOD OF CALCULATION: not described
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: not described - Effect data (Mortality): TLm small size fish : 13000 mg/l TLm medium size fish : 12750 mg/l TLm large size fish : 12500 mg/l - Concentration / response curve: not described - Effect concentration vs. test substance solubility: not described - Other effects: not described
Test condition:	TEST ORGANISMS - Strain: Raf. - Supplier: Pennsylvanian Fish Commission, Pennsylvania, USA - Wild caught: no - Age/size/weight/loading: size small : 3.88 cm - 0.96 gram size medium : 6.09 cm - 2.80 gram size large : 14.24 cm - 54.26 gram - Feeding: cooked shrimp - Pretreatment: not described - Feeding during test: no STABILITY OF THE TEST CHEMICAL SOLUTIONS: not described REFERENCE SUBSTANCE: no DILUTION WATER - Source: artificial - Aeration: artificial aeration - Alkalinity: not described - Hardness: not described - Salinity: not described - TOC: not described - TSS: not described - pH: not described - Oxygen content: 5 - 9 ppm - Conductance: not described - Holding water: artificial TEST SYSTEM - Test type: static

- Concentrations: not described
- Dosing rate: singlefold
- Renewal of test solution: no
- Exposure vessel type: glass jarrs
- Number of replicates, fish per replicate: 1, 5-10
- Test temperature: 19 - 21 degree C
- Dissolved oxygen: 5 - 9 ppm
- pH: not described
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described

DURATION OF THE TEST: 96 hours

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (21)

Type: static
Species: Poecilia latipinna (Fish, estuary)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 15996 -
Limit Test: no

Method: other: see freetext, method based on Freeman, L. "A standardized method for determining toxicity of pure compounds to fish", Sewage and Industrial wastes, 25, 7, 845 (1953)
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
96 hours static test. Test parameters were monitored, but not reported.
METHOD OF CALCULATION: not described
Median Tolerance Limit (TLm), not reported. Only up to 48 hours a TLm was determined.

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Mortality):

24 hours LC50 : 20040 mg/l

- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain: not described
- Supplier: Local pet shop
- Wild caught: no
- Age/size/weight/loading: not described
- Feeding: not described
- Pretreatment: not described
- Feeding during test: no

DILUTION WATER
- Source: reconstituted water
- Aeration: yes
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- TSS: not described
- pH: not described

- Oxygen content: not described
- Conductance: not described
- Holding water: reconsituted water
TEST SYSTEM
- Test type: static
- Concentrations: geometric series, not known
- Dosing rate: not described
- Renewal of test solution: no
- Exposure vessel type: not described
- Number of replicates, fish per replicate: 1, 10
- Test temperature: not described
- Dissolved oxygen: not described
- pH: not described
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described
DURATION OF THE TEST: 48 hours
TEST PARAMETER: Mortality

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (34)

Type: static
Species: Morone saxatilis (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring:
LC50: ca. 56000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Mortality):
24 hours LC50 : 450 mg/l
48 hours LC50 : 220 mg/l
72 hours LC50 : 110 mg/l
- Concentration / response curve: not determined
- Effect concentration vs. test substance solubility: not determined
- Other effects: not determined
RESULTS: CONTROL
- Number/percentage of animals showing adverse effects: not determined
- Nature of adverse effects: not determined

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (56)

Type: static
Species: Gambusia affinis (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 120 -
Limit Test: no

Method: other: see freetext
Year: 1980
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
96 hours static test. Test parameters were monitored, but

not reported.
METHOD OF CALCULATION:
LC50, method not described.

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain:
- Supplier: Local fish market
- Wild caught: no
- Age/size/weight/loading: not described/15-18 cm/5-10 gram/50 - 100 gram
- Feeding: oil cake
- Pretreatment: no
- Feeding during test: no

DILUTION WATER
- Source: obtained from upper lake of Bhopal
- Aeration: yes
- Alkalinity: 95.0 CaCO3
- Hardness: 84.0 mg CaCO3
- Salinity: not described
- TOC: not described
- TSS: Total dissolved solids : 160 mg/l
- pH: 8.3
- Oxygen content: 7.9 mg/l
- Conductance: not described
- Holding water: Upper lake of Bhopal

TEST SYSTEM
- Test type: static
- Concentrations: not described
- Dosing rate: not described
- Renewal of test solution: no
- Exposure vessel type: glass 40 liter
- Number of replicates, fish per replicate: 2, 10
- Test temperature: 30 degree C
- Dissolved oxygen: > 6.0 mg/l
- pH: not described
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described

DURATION OF THE TEST: 96 hours
TEST PARAMETER: Mortality

Reliability: (3) invalid
Test was performed in natural dilution water with relative high content of dissolved solids and sulfate. Effects of these solids are not known. pH and oxygen concentrations during test were not reported. This is a significant methodological deficiency, which makes documentation insufficient for assessment.

26-SEP-2005 (81)

Type: static
Species: Gambusia affinis (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 16500 -
Limit Test: no

Method: other: see freetext

Year:	1957
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED: Test was run in singlefold with 5 concentrations with turbid natural water (high concentration suspended solids) as test medium. METHOD OF CALCULATION: Median tolerance limit (TLm) was calculated based on dose-effect plot on log-paper.
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: nominal - Effect data (Mortality): 24 hours LC50 : 24000 mg/l 48 hours LC50 : 17500 mg/l 6 days LC50 : 10000 mg/l - Concentration / response curve: not described - Effect concentration vs. test substance solubility: not described - Other effects: possible adverse effects of high turbidity of test medium
Test condition:	TEST ORGANISMS - Wild caught: Stillwater Creek, Oklahoma, USA - Age/size/weight/loading: adult female - Feeding: Plancton/detritus, artificial food - Pretreatment: Tetramycin in holding tanks to prevent tail-rot - Feeding during test: no DILUTION WATER - Source: obtained from local farm ponds - Aeration: artificial aeration - Alkalinity: low < 100 ppm - Hardness: not described - Salinity: not described - TOC: not described - TSS: 650 mg/l (initial) and < 25 mg/l (final) - pH: 7.8 - 8.3 - Oxygen content: not described - Conductance: not described - Holding water: local farm ponds TEST SYSTEM - Test type: static - Concentrations: geometric series between 1000 and 56000 mg/l - Dosing rate: single-fold - Renewal of test solution: no - Exposure vessel type: pyrex cylindrical 15 liter vessel - Number of replicates, fish per replicate: 1, 10 - Test temperature: 22 - 25 degree C - Dissolved oxygen: not described - pH: 7.0 - 8.8 - Adjustment of pH: no - Intensity of irradiation: not described - Photoperiod: not described TEST PARAMETER : Mortality DURATION OF THE TEST: 6 days
Reliability:	(3) invalid The dilution water was turbid, which may have influenced the test result. Although sodium sulfate does not adsorb substantially on to soil particles, effects of turbidity can

not be excluded. Oxygen concentrations during test are not reported. This means that documentation is insufficient for assessment.

26-SEP-2005 (109)

Type:	static
Species:	Lepomis macrochirus (Fish, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: no
LC0:	= 8700 -
LC50:	= 13500 -
Limit Test:	no
Method:	other: see freetext
Year:	1954
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
Test performed in duplicate with five concentrations. Main testparameters determined during test. Defined dilution water used.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: Median tolerance limit determined using estimation from log dose-response plot.

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain: Raf.
- Supplier: private supplier Maryland, USA
- Wild caught: no
- Age/size/weight/loading: size 5 - 9 cm, weight 1 - 9 gram , on average 2.5 g/l
- Feeding: cooked shrimp
- Pretreatment: not described
- Feeding during test: no

DILUTION WATER
- Source: reconsituted water (Chu 14 modified)
- Aeration: yes
- Alkalinity: 36.8 - 37.0 mg/l ppm CaCO3
- Hardness: 37.4 - 40.6 mg/l ppm CaCO3
- Salinity: not described
- TOC: not described
- TSS: not described
- pH: 7.3 - 8.7
- Oxygen content: 4.4 - 8.9 ppm
- Conductance: 1.43x10-4 - 1.73x10-4 mhos 20 degree C
- Holding water: reconstituted water

TEST SYSTEM
- Test type: static
- Concentrations: 8700, 10000, 11500, 13500, 14000, 14500 mg/l
- Dosing rate: singlefold
- Renewal of test solution: no
- Exposure vessel type: Pyrex jarrs
- Number of replicates, fish per replicate: 2, 10
- Test temperature: 19 - 21 degree C

- Dissolved oxygen: 4.4 - 8.9 mg/l
- Alkalinity: 44 - 56 mg/l ppm CaCO3
- Hardness: 35 - 62 mg/l ppm CaCO3
- pH: 7.1 - 9.2
- Adjustment of pH: no
- Conductance: 60x10-4 -143x10-4
- Intensity of irradiation: not described
- Photoperiod: not described

DURATION OF THE TEST: 96 hours
TEST PARAMETER: Mortality

Reliability: (2) valid with restrictions
Although not all test criteria were met, results are reliable for assessment. Study with enough details.
Loading is not according to the guidelines, but because of aeration during the test this is not considered as having an impact on the test.
The low oxygen content (4.4 mg/l) had no impact on the fish considering the percentage of survival and oxygen content in the replicate.

26-SEP-2005 (98)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 13500 -
Limit Test: no

Method: other: see freetext, based on Cairns, J. et al, The effects of alkyl benzene sulfonate on aquatic organisms. Industrial Water and Wastes Journal, vol.9, no.1:22-28.
Year: 1968
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
static 96 hours test in reconstituted water.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described
- Reference substance: Potassium dichromate, TLm = 113 mg/l

Test condition: TEST ORGANISMS
- Strain: not described
- Supplier: not described
- Wild caught: not described
- Age/size/weight/loading: not described
- Feeding: not described
- Pretreatment: not described
- Feeding during test: no

DILUTION WATER
- Source: reconstituted water
- Aeration: yes
- Alkalinity: not described
- Hardness: not described
- Salinity: not described

- TOC: not described
- TSS: not described
- pH: not described
- Oxygen content: 5 - 9 ppm
- Conductance: not described
- Holding water: reconsituted water

TEST SYSTEM

- Test type: static
- Concentrations: geometric series, not known
- Dosing rate: not described
- Renewal of test solution: no
- Exposure vessel type: 18 liter vessels
- Number of replicates, fish per replicate: not described
- Test temperature: 16 - 20 degree C
- Dissolved oxygen: 5 - 9 ppm
- pH: not described
- Adjustment of pH:not described
- Intensity of irradiation: not described
- Photoperiod: not described

DURATION OF THE TEST: 96 hours
TEST PARAMETER: Mortality

Reliability: (2) valid with restrictions
When the result of Potassium dichromate (96 h, LC50) used as a reference substance, is compared with the result from another study (96 h, LC50 183 mg/l, Brachydanio rerio), it can be seen that it is in the same order of magnitude. This means that the result supports the accuracy of the result of the test substance, sodium sulfate.
This study would be considered as validity 3 because of the shortcomings. However, based on the other data, Sodium sulfate is a substance of very low toxicity and the results of this study confirm this, therefore this study is evaluated as valid with restrictions.

26-SEP-2005 (80)

Type: static
Species: Morone saxatilis (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring:
LC50: ca. 81000 -

Result:
RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Mortality):

24 hours LC50 : 650 mg/l
48 hours LC50 : 320 mg/l
72 hours LC50 : 160 mg/l

- Concentration / response curve:
- Effect concentration vs. test substance solubility:
- Other effects:

RESULTS: CONTROL
- Number/percentage of animals showing adverse effects:
- Nature of adverse effects:

RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (56)

Type: static
Species: Morone saxatilis (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring:
LC50: ca. 790000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Mortality):
24 hours LC50 : 790 mg/l
48 hours LC50 : 790 mg/l
72 hours LC50 : 790 mg/l
- Concentration / response curve:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS: CONTROL
- Number/percentage of animals showing adverse effects:
- Nature of adverse effects:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (56)

Type: static
Species: Morone saxatilis (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring:
LC50: ca. 1100000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Mortality):
24 hours LC50 : 1100 mg/l
48 hours LC50 : 1100 mg/l
72 hours LC50 : 1100 mg/l
- Concentration / response curve:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS: CONTROL
- Number/percentage of animals showing adverse effects:
- Nature of adverse effects:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (56)

Type: static
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: = 7960 -
Limit Test: no

Method: other: see freetext, based on EPA/600/4-90/027 (1991)

Year:	1997
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED: 96-hours static test in reconstituted water. STATISTICAL METHODS: logistic multiple regression METHOD OF CALCULATION: Probability regression model. measured values used for calculation whenever concentration was < 80% of initial concentration. ANALYTICAL METHODS: anion analyses by ion-chromatograpy
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: both - Effect data (Mortality): 24-hours LC50 : > 8080 mg/l 48 hours LC50 : > 7960 mg/l - Concentration / response curve: yes - Effect concentration vs. test substance solubility: no - Other effects: Not described RESULTS: CONTROL - Number/percentage of animals showing adverse effects: Not described - Nature of adverse effects: Not described
Test condition:	TEST ORGANISMS - Strain: not described - Supplier: ENSR, Fort Collins, CO, USA, in-house culture - Wild caught: no - Age/size/weight/loading: according to EPA, 1 to 7 days old - Feeding: yes, brine shrimp nauplii - Pretreatment: no - Feeding during test: yes, after 48 hours 100 microliter concentrated brine shrimp nauplii. DILUTION WATER - Source: reconstituted - Aeration: yes - Alkalinity: moderately - Hardness: not described - Salinity: not described - TOC: not described - TSS: not described - pH: 7.5 - 9.0 - Oxygen content: > 40% saturation - Conductance: not described - Holding water: tap water (purified by activated carbon) TEST SYSTEM - Test type: static - Concentrations: 4 concentrations with dilution factor 0.5 - Dosing rate: single-fold - Renewal of test solution: no - Exposure vessel type: plastic beakers 30 ml with 10 ml of water - Number of replicates, fish per replicate: 3-5, 5 - Test temperature: 25 degree C - Dissolved oxygen: > 40% saturation - pH: 7.5 - 9 - Adjustment of pH: no - Intensity of irradiation: not described - Photoperiod: not described DURATION OF THE TEST: 96 hours TEST PARAMETER: mortality SAMPLING: no

MONITORING OF TEST SUBSTANCE CONCENTRATION: yes
Reliability: (2) valid with restrictions
Test performed according to standardized EPA guideline for testing of effluents, with determination of test concentrations. Test parameters pH and oxygen measured but not all reported. No information about survival in controls. Replicate test performance.
Flag: Critical study for SIDS endpoint
26-SEP-2005 (71)

Type: static
Species: other: Morone saxatilis (striped bass, fingerlings)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 3500 -

Test substance: other TS:Na2SO4 tech. grade
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (56)

Type: static
Species: other: Morone saxatilis ,striped bass, larvea
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 250 -

Test substance: other TS:Na2SO4 tech. grade
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (56)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
LC0: = 15000 -

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (65)

Species: Gambusia affinis (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 17500 -

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (36)

Species: Lepomis gibbosus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 13500 -

Reliability: (4) not assignable

Reference not available

13-JUN-2003 (83)

Species:	Lepomis macrochirus (Fish, fresh water)
Exposure period:	24 hour(s)
Unit:	mg/l Analytical monitoring: no
LC50:	= 17500 -
Limit Test:	no
Method:	other: see freetext, method based on Freeman, L. "A standardized method for determining toxicity of pure compounds to fish", Sewage and Industrial wastes, 25, 7, 845 (1953)
Year:	1965
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED: 96 hours static test. Test parameters were monitored, but not reported. METHOD OF CALCULATION: not described Median Tolerance Limit (TLm), not reported. Only a 24 hours TLm was determined.
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: nominal - Effect data (Mortality): - Concentration / response curve: not described - Effect concentration vs. test substance solubility: not described - Other effects: not described
Test condition:	TEST ORGANISMS - Strain: not described - Supplier: Local pet shop - Wild caught: no - Age/size/weight/loading: not described - Feeding: not described - Pretreatment: not described - Feeding during test: no DILUTION WATER - Source: reconstituted water - Aeration: yes - Alkalinity: not described - Hardness: not described - Salinity: not described - TOC: not described - TSS: not described - pH: not described - Oxygen content: not described - Conductance: not described - Holding water: reconsituted water TEST SYSTEM - Test type: static - Concentrations: geometric series, not known - Dosing rate: not described - Renewal of test solution: no - Exposure vessel type: not described - Number of replicates, fish per replicate: 1, 10 - Test temperature: not described - Dissolved oxygen: not described - pH: not described - Adjustment of pH: not described - Intensity of irradiation: not described

- Photoperiod: not described
DURATION OF THE TEST: 96 hours
TEST PARAMETER: Mortality

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (34)

Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: ca. 13500 - 14500

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (36)

Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC100: = 7000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
24 hours: LC50 705 mg/l
- Effect data (Mortality):
- Concentration / response curve:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS: CONTROL
- Number/percentage of animals showing adverse effects:
- Nature of adverse effects:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (65)

Species: other: Cyprinus carpio
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
LC0: < 2000 -

Reliability: (4) not assignable
Reference not translated

26-SEP-2005 (99)

Species: other: Notropis spilopterus
Exposure period: 120 hour(s)
Unit: mg/l Analytical monitoring:
MLc : = 100 -

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (105)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:	static
Species:	Daphnia magna (Crustacea)
Exposure period:	48 hour(s)
Unit:	mg/l Analytical monitoring: no
EC50:	= 9124 -
Limit Test:	no
Method:	other: see freetext
Year:	1995
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: 48-hours static test in reconstituted water.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described
ANALYTICAL METHODS: no

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Immobilisation): not described
- Concentration / response curve: not described
- Cumulative immobilisation: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Breeding method: in-house in reconsituted water
- Age: < 24 hours
- Feeding: no
- Pretreatment: not described
- Feeding during test: no
- Control group: yes

DILUTION WATER
- Source: reconstituted water
- Aeration: not described
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- Ca/Mg ratio: not described
- Na/K ratio: not described
- TSS: not described
- pH: not described
- Oxygen content: not described
- Conductance: not described
- Holding water: reconstituted water

TEST SYSTEM
- Test type: semi-static
- Concentrations: not described
- Renewal of test solution: yes
- Exposure vessel type: 100 ml solution
- Number of replicates, individuals per replicate: 2, 10
- Test temperature: 20 degree C

- Dissolved oxygen: not described
- pH: not described
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: dark

DURATION OF THE TEST: 48 hours
TEST PARAMETER: immobility
SAMPLING: no
MONITORING OF TEST SUBSTANCE CONCENTRATION: no

Reliability: (3) invalid
documentation was insufficient for assessment

26-SEP-2005 (8)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: = 2564 -
Limit Test: no

Method: other: see freetext, based on Anderson, B.G. et al. The evaluation of aquatic invertebrates as assay organisms for the determination of the toxicity of industrial wastes. Report of the Ohio State University (1948)
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
48 - 96 hours static test. Test parameters were monitored, but not reported.
METHOD OF CALCULATION: not described
Median Tolerance Limit (TLm), not reported.

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Immobilisation):
24 hours EC50 : 8384 mg/l
72 hours EC50 : 725 mg/l
96 hours EC50 : 630 mg/l
- Concentration / response curve: not described
- Cumulative immobilisation: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain: not described
- Source/supplier: Put-In Bay, Ohio, USA
- Breeding method: In-house, not described
- Age: not defined, but designated as a) young, b) adult.
- Feeding: not described
- Pretreatment: not described
- Feeding during test: no
- Control group: not described

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (34)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: yes
EC50: = 4580 -
Limit Test: no

Method: other: see freetext, based on EPA/600/4-90/027 (1991)

guideline
Year: 1997
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: 48-hours static test in reconstituted water.
STATISTICAL METHODS: logistic multiple regression
METHOD OF CALCULATION: Probability regression model. Measured values used for calculation whenever concentration was < 80% of initial concentration.
ANALYTICAL METHODS: anion analyses by ion-chromatograpy

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: both
- Effect data (Immobilisation):
24 hours EC50 : 6290 mg/l
- Concentration / response curve: yes
- Cumulative immobilisation: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain: not described
- Source/supplier: ENSR, Fort Collins, CO, USA
- Breeding method: in-house in reconsituted water at 20 degree C
- Age: < 24 hours
- Feeding: yeast/cerophyl/trout chow (YCT)
- Pretreatment: no
- Feeding during test: yes, 100 microliter concentrated algae/ YCT 1:1 mixture at start test
- Control group: yes
DILUTION WATER
- Source: reconstituted hard water (EPA)
- Aeration: yes
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- Ca/Mg ratio: not described
- Na/K ratio: not described
- TSS: not described
- pH: 7.5 - 9.0
- Oxygen content: > 40% of saturation value
- Conductance: not described
- Holding water: reconstituted water (hard, EPA)
TEST SYSTEM
- Test type: static
- Concentrations: 4 concentrations in geometric series with factor 0.5
- Renewal of test solution: no
- Exposure vessel type: plastic vessels 30 ml with 10 ml dilution water.
- Number of replicates, individuals per replicate: 3-5, 5
- Test temperature: 20 degree C
- Dissolved oxygen: > 40% saturation
- pH: 7.5 - 9.0
- Adjustment of pH: no
- Intensity of irradiation: not described
- Photoperiod: 16:8 hour light-dark
DURATION OF THE TEST: 48 hours

TEST PARAMETER: immobility
SAMPLING: no
MONITORING OF TEST SUBSTANCE CONCENTRATION: yes

Reliability: (2) valid with restrictions
Test performed according to standardized EPA guideline for testing of effluents, with determination of test concentrations. Test parameters pH and oxygen measured but not all reported. No information about controls. Replicate test performance.

Flag: Critical study for SIDS endpoint

26-SEP-2005 (71)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: = 4547 -
Limit Test: no

Method: other:see freetext
Year: 1953
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: A 100 hours static test with 9 concentrations in three-fold.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: Toxicity Threshhold, defined by Anderson et al., Report by Ohio State Univ. Research Found. To Amer. Petrol. Inst., New York, N.Y. (1948). Toxicity Threshold is comparable with LC50 value.
ANALYTICAL METHODS: not described

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Immobilisation):
- Concentration / response curve: not described
- Cumulative immobilisation: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain: not described
- Source/supplier: West Virginia University, USA
- Breeding method: in-house
- Age: < 12 hours
- Feeding: yeast
- Pretreatment: not described
- Feeding during test: no
- Control group: yes

DILUTION WATER
- Source: reconstituted water
- Aeration: not described
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- Ca/Mg ratio: not described
- Na/K ratio: not described
- TSS: not described
- pH: not described
- Oxygen content: not described

- Conductance: not described
- Holding water: reconsituted water
TEST SYSTEM
- Test type: static
- Concentrations: 9 concentrations, not defined
- Renewal of test solution: no
- Exposure vessel type: pyrex vessels, 100 ml
- Number of replicates, individuals per replicate: 3, 10
- Test temperature: 22 - 24 degree C
- Dissolved oxygen: not described
- pH: < 7.7
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described
DURATION OF THE TEST: 100 hours
TEST PARAMETER: Immobility

Reliability: (3) invalid
Documentation insufficient for assessment
26-SEP-2005 (36)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC50: = 2564 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Immobilisation):
24 hours EC50 : 8384 mg/l
- Concentration / response curve:
- Cumulative immobilisation:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (33)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC100: = 5200 -

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (65)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Chlorella pyrenoidosa (Algae)
Exposure period: 8 day(s)
Unit: mg/l Analytical monitoring:
EC100 : = 57700 -

Method: other

Reliability: (4) not assignable
Reference not translated
26-SEP-2005 (77)

Species: other algae: Nitzschia linearis
Exposure period: 120 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: = 1900 -
Limit Test: no

Method: other: see freetext, based on Cairns J. et al. Industrial water and Wastes Journal. 9 (1), 22-28 (1964).
Year: 1968
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
a static 120 hours test in defined test medium.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: Median tolerance limit (TLm) method not defined.
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data/Element values: growth (cell counts)
- Cell density data: not described
- Growth curves: not described
- Reference substance: Potassium dichromate, TLm = 0.208 mg/l

Test condition: TEST ORGANISMS
- Strain: W.Sm.
- Source/supplier: not described
- Laboratory culture: not described
- Method of cultivation: not described
- Pretreatment: no
- Controls: yes
- Initial cell concentration: not described

DILUTION WATER
- Source: reconstituted water
- Aeration: not described

TEST SYSTEM
- Test type: static
- Concentrations: geometric series
- Renewal of test solution: no
- Exposure vessel type: 150 ml glass
- Number of replicates: not described
- Concentrations: not described
- Test temperature: 16 - 22 degree C
- pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described

TEST PARAMETER: growth

Reliability: (2) valid with restrictions
In this test a different algae species is used than recommended in the OECD-guidelines. When the results of Potassium dichromate (72 h, EbC50) used as a reference substance, are compared with the results given in the EC-directive 92/69/EEC (mean 0.53 mg/l, range 0.20 - 0.75 mg/l) the sensitivity of Nitzschia linearis is not

significantly different from that of Selenastrum capricornutum or Scenedesmus subspicatus.

It is recognised that the duration of this study was greater than the recommended OECD study time but as the reference result from this study is on the lower boundary of the EC recommendation, the two results are considered comparable.

This study would be considered as validity 3 because of the shortcomings. However, based on the other data, Sodium sulfate is a substance of very low toxicity and the results of this study confirm this, therefore this study is evaluated as valid with restrictions (2).

Flag: Critical study for SIDS endpoint

26-SEP-2005 (80)

Species: other aquatic plant: Myrophilium spicatum (Eurasian watermilfoil)
Endpoint: other: root weight
Exposure period: 32 day(s)
Unit: mg/l Analytical monitoring: no
EC50: = 10228 -
EC50 shoot length :
= 4120 -
EC50 shoot weight :
= 9376 -
EC50 root length :
= 10370 -
Limit Test: no

Method: other: see freetext
Year: 1974
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
A 32 days test with plants cultivated in liquid/soil medium under continuous illumination.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: root weight and shoot length, quotient of effect of test substance added in soil fraction and effect of test substance added to water phase, corrected for control effect
ANALYTICAL METHODS: not described

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data/Element values: not described
- Cell density data: not described
- Growth curves: yes

Test condition: TEST ORGANISMS
- Strain: L.
- Source/supplier: Clone from Friesland, The Netherlands
- Laboratory culture: yes
- Method of cultivation: cultivated in greenhouse in woods earth/ferric silicate/tap water mixture
- Pretreatment: CuSO4 to reduce algae growth
- Controls: yes
- Initial cell concentration: not described

DILUTION WATER
- Source: Tap water
- Aeration: no

GROWTH/TEST MEDIUM CHEMISTRY
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- EDTA: not described
- TSS: not described
- pH: not described
- Dissolved oxygen: not described

TEST SYSTEM
- Test type: static
- Concentrations: not described
- Renewal of test solution: not described
- Exposure vessel type: flatt-bottom tubes 200 ml
- Number of replicates: 10
- Concentrations: not described
- Test temperature: 20 degree C
- pH: not described
- Intensity of irradiation: 300 fc
- Photoperiod: continuous

TEST PARAMETER: root weight and shoot length

Reliability: (3) invalid
Non-standardized test method, and insufficient documentation

26-SEP-2005 (92)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type:	aquatic
Species:	activated sludge
Exposure period:	37 day(s)
Unit:	g/l Analytical monitoring:
NOEC:	ca. 26 -
Method:	other: see freetext
Year:	1986
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4

Test condition: TEST ORGANISMS
- Bacteria in activated sludge
- Supplier: obtained from a local municipal wastewater treatment plant.
- Pretreatment: acclimated for a period of over a month.
- Substrate: synthetic substrate

TEST SYSTEM

- Concentrations: concentrations were increased from 8 to 35 g/l over a time period of 37 days. Concentration steps were 2 - 5 g/l.
- Exposure vessel: 10 l reactor of which 8 l were aeration chamber and 2 l settling basin.
- Analyses: BOD, COD, TSS etc. analyses were done according to APHA standard methods.
- Dissolved oxygen: 6 - 8 mg/l
- Temperature: 18.5 - 22.5 degree C

Reliability: (2) valid with restrictions
Although it is not a standard test and not all test parameters were reported, the results are reliable for assessment. Study with enough details.

26-SEP-2005 (95) (96)

Type: aquatic
Species: activated sludge
Exposure period: 37 day(s)
Unit: g/l Analytical monitoring:
NOEC: ca. 26 -

Method: other: see freetext
Year: 1986
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Test condition: TEST ORGANISMS
- Motile protozoa in activated sludge
- Supplier: obtained from a local municipal wastewater treatment plant.
- Pretreatment: acclimated for a period of over a month.
- Substrate: synthetic substrate
TEST SYSTEM
- Concentrations: concentrations were increased from 8 to 35 g/l over a time period of 37 days. Concentration steps were 2 - 5 g/l.
- Exposure vessel: 10 l reactor of which 8 l were aeration chamber and 2 l settling basin.
- Analyses: BOD, COD, TSS etc. analyses were done according to APHA standard methods.
- Dissolved oxygen: 6 - 8 mg/l
- Temperature: 18.5 - 22.5 degree C

Reliability: (2) valid with restrictions
Although it is not a standard test and not all test parameters were reported, the results are reliable for assessment. Study with enough details.

26-SEP-2005 (95) (96)

Type: aquatic
Species: activated sludge
Exposure period: 37 day(s)
Unit: g/l Analytical monitoring:
NOEC: ca. 8 -

Method: other: see freetext
Year: 1986
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Test condition: TEST ORGANISMS
- Stalked ciliates in activated sludge
- Supplier: obtained from a local municipal wastewater treatment plant.
- Pretreatment: acclimated for a period of over a month.
- Substrate: synthetic substrate
TEST SYSTEM
- Concentrations: concentrations were increased from 8 to 35 g/l over a time period of 37 days. Concentration steps were 2 - 5 g/l.
- Exposure vessel: 10 l reactor of which 8 l were aeration chamber and 2 l settling basin.
- Analyses: BOD, COD, TSS etc. analyses were done according to APHA standard methods.
- Dissolved oxygen: 6 - 8 mg/l
- Temperature: 18.5 - 22.5 degree C

Reliability: (2) valid with restrictions
Although it is not a standard test and not all test parameters were reported, the results are reliable for assessment. Study with enough details.

26-SEP-2005 (95) (96)

Type: aquatic
Species: activated sludge
Exposure period: 40 day(s)
Unit: g/l Analytical monitoring:
NOEC: ca. 30 -

Method: other: see freetext
Year: 1980
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Test condition: TEST ORGANISMS
- Activated sludge
- Supplier: not described
- Pretreatment: not described
- Substrate: not described
TEST SYSTEM
- Concentrations: concentrations were increased from 10 to 40 g/l over a time period of ca. 40 days. Concentration steps were 10 g/l.
- Exposure vessel: 10 l
- Analyses: effluent analyses were done according to APHA standard methods.
- pH: 7 - 7.5
- Temperature: 20 - 23 degree C
- Dissolved oxygen: 2.3 - 3.5 mg/l

Reliability: (2) valid with restrictions
Although it is not a standard test and not all test parameters were reported, the results are reliable for assessment. Study with enough details.

26-SEP-2005 (40)

Type: aquatic
Species: Pseudomonas fluorescens (Bacteria)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = 10000 -

Method: other: Bestimmung der biologichen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L8 (1968) modifiziert

Reliability: (4) not assignable
Reference not available

13-JUN-2003 (14)

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 16 hour(s)
Unit: mg/l Analytical monitoring:
EC10: > 1000 -

Method: other: DIN 38412 Teil 8

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (55)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

Species:	other: Lymnaea (Pond snail)
Endpoint:	Mortality
Expos. period:	96 other: hours
Unit:	other: mg/l
LC50:	= 1151 -
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: - Effect data (Immobilisation): 24 hours LC50 : 1750 mg/l 48 hours LC50 : 1750 mg/l 72 hours LC50 : 1750 mg/l - Concentration / response curve: - Cumulative immobilisation: - Effect concentration vs. test substance solubility: - Other effects: RESULTS CONTROL: RESULTS: TEST WITH REFERENCE SUBSTANCE - Concentrations: - Results:
Reliability:	(4) not assignable Reference not available

26-SEP-2005 (33)

Species:	other: Lymnaea (Pond snail)
Endpoint:	Mortality
Expos. period:	96 other: hours
Unit:	other: mg/l
LC50:	= 799 -
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: - Effect data (Immobilisation): 24 hours LC50 : 1215 mg/l 48 hours LC50 : 1215 mg/l 72 hours LC50 : 1215 mg/l - Concentration / response curve: - Cumulative immobilisation: - Effect concentration vs. test substance solubility: - Other effects: RESULTS CONTROL: RESULTS: TEST WITH REFERENCE SUBSTANCE - Concentrations: - Results:
Reliability:	(4) not assignable

Reference not available
26-SEP-2005 (33)

Species: other: Ophryotrocha labronica (Polychaete)
Endpoint: Mortality
Expos. period: 20 other: hours
Unit: other: mg/l
LC50: = 5.4 -

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (85)

Species: other: Lymneae sp. (eggs)
Endpoint: Mortality
Expos. period: 96 other: hour(s)
Unit: other: mg/l
LC50: = 3553 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Immobilisation):
24 hours LC50 : 5401 mg/l
48 hours LC50 : 5400 mg/l
72 hours LC50 : 5400 mg/l
- Concentration / response curve:
- Cumulative immobilisation:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (3) invalid
Documentation insufficient for assessment
26-SEP-2005 (34)

Species: other: Trycorythus sp.
Endpoint: Mortality
Expos. period: 96 other: hours
Unit: other: g/l
LC50: = .66 -

Method: other: see freetext
Year: 1996
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: 96-hours acute semi static test in river water.
STATISTICAL METHODS: one-way ANOVA
METHOD OF CALCULATION: probit analysis
ANALYTICAL METHODS: nutrient concentrations by spectrophotometer
Full chemical analyses by ICP-ES, AAS and autoanalyzer
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Immobilisation):
96 hours LC50 : 0.66 g/l

NB. The probit analysis could not be used since there was no normal distribution of concentration response data.
- Concentration / response curve: no
- Cumulative immobilisation: yes
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Source/supplier: Sabie river, Kruger national park, South Africa
- Pretreatment: 25 individuals were acclimated unfed per raceway for 36 h. All dead animals were removed and numbers were equalized between the raceways, before addition of salt solutions.
- Feeding during test: no
- Control group: yes

DILUTION WATER
- Source: Sabie river water
- Salinity: not described
- TOC: not described
- Ca/Mg ratio: not described
- Na/K ratio: not described
- TSS: not described
- pH: not described

Conductance: not described
- Holding water: Sabie river water

TEST SYSTEM
- Test type: semi static
- Concentrations: 4 concentrations, 0.20, 0.66, 1.46 and 4.40 g/l.
- Renewal of test solution: yes, 20% of the water was replaced daily.
- Exposure vessel type: 12.5 l perspex experimental stream system; raceways. Four kaolinite stones were placed in the channel to serve as a substrate.
- Number of replicates, individuals per replicate: 3, not known
- Current: 0.75 or 1 m/s
- Test temperature: 9-16 degree C
- Dissolved oxygen: 65.0-105.0% saturation
- pH: 6.93-7.20
- Adjustment of pH: no
- Aeration: no
- Alkalinity: 62-101 mg/l
- Hardness: approx. 69.4 mg/l
- Intensity of irradiation: not described
- Photoperiod: 12:12 hour light-dark

DURATION OF THE TEST: 96 hours
TEST PARAMETER: immobility

Reliability: (2) valid with restrictions
No standard test, but test with a lot of detailed information. The test results did not give a normal dose respons curve.

Flag: Critical study for SIDS endpoint
26-SEP-2005 (42)

4.6.2 Toxicity to Terrestrial Plants

Species: other terrestrial plant: Capsicum annuum L.
Endpoint: other: Number and size of fruit

Expos. period: 4 month

Method: other: see freetext
Year: 2000
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A 4 months test in a greenhouse.
- Endpoints: Fruit was collected at ripening (at the red stage) and weight, total number and yield were recorded.
STATISTICAL METHOD
Data were statistically analysed by ANOVA.

Result: RESULTS
- Effect data:
Fruit number: Increased with concentration
Fruit size: decreased with concentration
Yield: decreased with concentration
Fructose, glucose and amino acids significantly decreased with higher concentrations.
The pulp thickness became less with increasing concentration.

Test condition: TEST SPECIES
- Capsicum annuum L.
- Source: not known
- pretreatment: No
- Substrate: Hoagland nutrient solution
TEST SYSTEM
- Concentrations: 2 (control), 3, 4, 6 and 8 dS/m solution (this is 0, 6.1, 12.2, 24.1 and 36.7 mM Sodium sulfate) in Hoagland nutrient solution.
- Test vessel: 120 l container
- Number of plants per replicate: 1
- Replicates: 5
- Temperature: 18-35 degree Celsius
- Relative humidity: 55-75%
- pH: 5.5-6.0
- Photoperiod: not known
- Watering: daily addition of deionized water
- Solutions were analysed weekly and readjusted to initial nutrient concentrations

Reliability: (3) invalid
No standard method. The method is described in detail but the results are not in much detailed. It is not clear at what concentration a significant decrease or increase occurs.

26-SEP-2005 (72)

Species: other terrestrial plant: Picea glauca
Endpoint: other: emergence, survival, shoot and root length, number of lateral roots, leaf necrosis, fresh weight and photosynthesis
Expos. period: 42 day(s)

Method: other: see freetext
Year: 2000
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A six weeks test in sand.
- Endpoints: Percentage emergence was noted daily. After six

weeks survival, leaf necrosis, shoot and root length, number of lateral roots, fresh weight and photosynthesis were recorded.
Photosynthesis was determined spectrophotometrically from methanol extract and calculated using MacKinney equation.
STATISTICAL METHOD
- Emergence data was analyzed using a general linear model (GLM) repeated measure technique.
- Growth data were analyzed with a glm using one-way ANOVA.
- The means were compared using Duncan's multiple range test.

Result: RESULTS
- Effect data:
Emergence: percentage germination was significantly less in 20 mM and higher
Survival: significant decrease at 50 mM and higher
Root length: significant reduction in length from 20 mM and higher
Number of lateral roots: significant decrease from 50 mM and higher
Leaf necrosis: significant necrosis in 50 mM and higher
Fresh weight: reduction in 50 mM and higher
Photosynthesis: Chlorophyll content did not change compared to the control

Test condition: TEST SPECIES
- Picea glauca
- Source: Pine Ridge Nursery, Alberta, Canada (seedlot DL 68-12-4-83)
- pretreatment: No
- Substrate: quartz-feldspar sand (particle size range 0.19-3 mm)
TEST SYSTEM
- Concentrations: 0, 10, 20, 50, 100 and 250 mM solution in deionized water.
- Test vessel: 4 l germination trays.
- Number of seeds per replicate: 40
- Replicates: 5 trays per concentration.
- Moisture content of sand: 13%
- Thermoperiod: 20/15 degree Celsius
- Photoperiod: 18 hours
- High humidity was obtained by covering the trays with transparant plastic lids
- After two weeks the lids were removed
- Watering: Every other day after removing the lids, 500 ml of deionized water was sprayed over the sand. Every seven days 50 ml of Hoagland's mineral solution was sprayed on the sand.

Reliability: (2) valid with restrictions
No standard method, but study with enough details.

26-SEP-2005 (28)

Species: other terrestrial plant: Pinus banksiana
Endpoint: other: emergence, survival, shoot and root length, number of lateral roots, leaf necrosis, fresh weight and photosynthesis
Expos. period: 42 day(s)

Method: other: see freetext
Year: 2000
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method:	METHOD FOLLOWED A six weeks test in sand. - Endpoints: Percentage emergence was noted daily. After six weeks survival, leaf necrosis, shoot and root length, number of lateral roots, fresh weight and photosynthesis were recorded. Photosynthesis was determined spectrophotometrically from methanol extract and calculated using MacKinney equation. STATISTICAL METHOD - Emergence data was analyzed using a general linear model (GLM) repeated measure technique. - Growth data were analyzed with a glm using one-way ANOVA. - The means were compared using Duncan's multiple range test.
Result:	RESULTS - Effect data: Emergence: germination was significantly enhanced at 20 mM. At 250 mM the germination was only 7% Survival: significant decrease at 50 mM and higher Shoot length: significant reduction in 50 mM and higher Root length: significant reduction in length from 10 mM and higher Number of lateral roots: significant decrease from 10 mM and higher Leaf necrosis: significant from 50 mM on Fresh weight: reduction in 50 mM and higher Photosynthesis: Chlorophyll content did not change compared to the control
Test condition:	TEST SPECIES - Pinus banksiana - Source: Pine Ridge Nursery, Alberta, Canada (seedlot SJ 75-15-4-77) - pretreatment: No - Substrate: quartz-feldspar sand (particle size range 0.19-3 mm) TEST SYSTEM - Concentrations: 0, 10, 20, 50, 100 and 250 mM solution in deionized water. - Test vessel: 4 l germination trays. - Number of seeds per replicate: 40 - Replicates: 5 trays per concentration. - Moisture content of sand: 13% - Thermoperiod: 20/15 degree Celsius - Photoperiod: 18 hours - High humidity was obtained by covering the trays with transparant plastic lids - After two weeks the lids were removed - Watering: Every other day after removing the lids, 500 ml of deionized water was sprayed over the sand. Every seven days 50 ml of Hoagland's mineral solution was sprayed on the sand.
Reliability:	(2) valid with restrictions No standard method, but study with enough details.
26-SEP-2005	(28)
Species:	other terrestrial plant: Picea mariana
Endpoint:	other: emergence, survival, shoot and root length, number of lateral roots, leaf necrosis, fresh weight and photosynthesis
Expos. period:	42 day(s)
Method:	other: see freetext

Year:	2000
GLP:	no data
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED A six weeks test in sand. - Endpoints: Percentage emergence was noted daily. After six weeks survival, leaf necrosis, shoot and root length, number of lateral roots, fresh weight and photosynthesis were recorded. Photosynthesis was determined spectrophotometrically from methanol extract and calculated using MacKinney equation. STATISTICAL METHOD - Emergence data was analyzed using a general linear model (GLM) repeated measure technique. - Growth data were analyzed with a glm using one-way ANOVA. - The means were compared using Duncan's multiple range test.
Result:	RESULTS - Effect data: Emergence: percentage germination was significantly less in 100 mM. Survival: significant decrease at 100 mM and higher Shoot length: significant reduction in 50 mM and higher Root length: significant reduction in length from 20 mM and higher Number of lateral roots: significant decrease from 50 mM and higher Leaf necrosis: no significant necrosis Fresh weight: reduction in 50 mM and higher Photosynthesis: Chlorophyll content did not change compared to the control
Test condition:	TEST SPECIES - Picea mariana - Source: Pine Ridge Nursery, Alberta, Canada (seedlot MW 61-13-5-9) - pretreatment: No - Substrate: quartz-feldspar sand (particle size range 0.19-3 mm) TEST SYSTEM - Concentrations: 0, 10, 20, 50, 100 and 250 mM solution in deionized water. - Test vessel: 4 l germination trays. - Number of seeds per replicate: 40 - Replicates: 5 trays per concentration. - Moisture content of sand: 13% - Thermoperiod: 20/15 degree Celsius - Photoperiod: 18 hours - High humidity was obtained by covering the trays with transparant plastic lids - After two weeks the lids were removed - Watering: Every other day after removing the lids, 500 ml of deionized water was sprayed over the sand. Every seven days 50 ml of Hoagland's mineral solution was sprayed on the sand.
Reliability:	(2) valid with restrictions No standard method, but study with enough details.

26-SEP-2005 (28)

Species:	other terrestrial plant: Medicago sativa L.
Endpoint:	other: plant growth, nodule number and weight
Method:	other: see freetext
Year:	1995
GLP:	no data
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED A 55 days test in a greenhouse. - Endpoints: Plant dry weight and nodule number and dry weight. STATISTICAL METHOD Data were statistically analysed by ANOVA.
Result:	RESULTS - Effect data: Plant growth: decreased with concentration, dry weight was 50% of control at 130 mOsm at the end of the test. Nodule specific weight: did not change much at any osmotic level Number of nodules: decreased with concentration, 71% reduction in the highest concentration.
Test condition:	TEST SPECIES - Medicago sativa L. - Source: not known - pretreatment: seeds were surface-steriized with 70% ethanol for 7 minutes, rinsed in sterile distilled water, and allowed to germinate on 1% water agar for 20 h. 10 germinated seeds were planted in a sterile-modified Leonard jar containing sand, and inoculated with R. meliloti. Plants were thinned out to 5 plants per jar, 14 days after planting. - Substrate: Hoagland nutrient solution TEST SYSTEM - Concentrations: 0, 70, 130, 200 or 250 mOsm in N-free nutrient solution. Salt was added 72 h after planting and checked weekly - Number of plants per replicate: 5 - Replicates: 6 - Temperature: 27/21 degree Celsius (day/night) - Relative humidity: not known - Photoperiod: 14 h - Plants were watered every following day - Watering: daily addition of deionized water - Solutions were analysed weekly and readjusted to initial nutrient concentrations
Reliability:	(3) invalid No standard method. The method is described in detail but the results are not in much detailed. It is not clear at what concentration a significant decrease or increase occurs.

26-SEP-2005 (11)

Species:	other terrestrial plant: Altriplex prostrata
Endpoint:	other: survival, height, nodes, branches, leaves, dry mass and photosynthesis
Expos. period:	1 month
Method:	other: see freetext
Year:	1996
GLP:	no

Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A one month semi static test in defined test medium.
- Endpoints: Plant height, number of leaves, nodes and branches were recorded weekly. Photosynthesis was measured once before harvesting and dry mass was determined after one month.
Photosynthesis was measured using a infra-red gas analyzer.
STATISTICAL METHOD
Two-way ANOVA was used to determine differences among treatments.
The Bonferroni test was used for other comparisons.

Result: RESULTS
- Effect data:
Survival: All plants survived in every concentration
Plant height: The height decreased as osmotic potential was lowered
Number of nodes: The number decreased as osmotic potential was lowered
Number of branches: The number decreased as osmotic potential was lowered
Number of leaves: The number decreased from -1.00 MPa on
Dry mass: Mass decreased from -1.00 MPa on
Photosynthesis: Photosynthesis decreased from -1.00 MPa on

Test condition: TEST SPECIES
- Atriplex prostrata
- Source: Salt marsh in Rittman, Ohio (Wayne county)
- Size of seeds: 1.5-2.0 mm diameter
- pretreatment: Seeds were germinated in an incubator.
12h thermoperiod of 5:25 degree celcius.
12h photoperiod 20.0 micromol/m2/s, 400-700 nm.
Acclimated to greenhouse conditions for two days in individual pots. Grown for 15 days under natural light conditions. Plants were acclimated to the test solutions by placing them at lower osmotic potential every two days until the final osmotic potential was reached
- Substrate: Sand
TEST SYSTEM
- Concentrations: 0.00, -0.75, -1.00 and -1.50 MPa solution, dissolved in half strength Hoagland and Arnon's no. 2 solution. Solutions were replaced after two weeks.
- Test vessel: 9x9 cm black plastic pots.
- Replicates: 10 per concentration.

Reliability: (3) invalid
Study with a lot of details on the method, but in the results no statistics is mentioned. It is not clear were significant differences were found.

26-SEP-2005 (35)

4.6.3 Toxicity to Soil Dwelling Organisms

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

Species:	other: Culex (Mosquito)
Endpoint:	mortality
Expos. period:	48 hour(s)
Unit:	other: mg/l
LC50:	= 4325 -

Result: RESULTS: EXPOSED
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (33)

Species: other: Culex (Mosquito)
Endpoint: mortality
Expos. period: 48 hour(s)
Unit: other: mg/l
LC50: = 3004 -

Result: RESULTS: EXPOSED
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (33)

Species: other: Culex sp. larvea
Endpoint: mortality
Expos. period: 48 hour(s)
Unit: other: mg/l
LC50: = 13350 -

Method: METHOD FOLLOWED: not described in detail.
METHOD OF CALCULATION:
not described
Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Immobilisation):
24 hours LC50 : 11430 mg/l
- Concentration / response curve:
- Cumulative immobilisation:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (3) invalid
Documentation insufficient for assessment
26-SEP-2005 (34)

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

Memo: TOXICITY TO FISH

Remark: Method:
Acute toxicity to Lake Emerald shiner (Notropis a. atherinoides) and spotfin shiner (Notropis spilopterus). 96 hours testing according to Powers, E.B. Biol. Monograpgs IV, No. 2 pp.1-73 (1917). 18 degree C in 2-liter vessels. Oxygen > 4 mg/l.

Results:
Minimum Lethal Concentration (NOEC) : 100.0 mg/l for both fish. 100% survival in controls.

26-SEP-2005 (106)

Memo: TOXICITY TO INVERTEBRATES

Remark: Method:
Static bioassay, 28.5 +/-1.5 degree C:
Effect parameters determined graphically. Tests with three replications + control. Dilution water: Unchlorinated bore-hole water.,pH=7, DO 7.5 mg/l, alkalinity 110 mg/l CaCO3.
Results: 96h; LC 100 - LC 50 - LC 0 (mg/l).
Branchiura sowerbyi (worm) 12000 - 7700 - 4750
Cyclops viridis (plankton) 4500 - 2000 - 1000
Lymnaea luteola (mollusc) 9500 - 8250 - 4000

15-OCT-2001 (44)

Memo: TOXICITY TO INVERTEBRATES

Remark: Method:
Static test with Daphnia magna, 48 hours in Lake Erie (USA) water. Method according to Anderson, B.G. Sewage Works J. 16(6):1156-1165 (1944).
Results:
Threshold concentration for immobilization:
5960 mg/l (16 hours)
7105 mg/l (48 hours)

15-OCT-2001 (6)

Memo: TOXICITY TO INVERTEBRATES

Remark: Marine invertebrates; salinity of sea water 30g/kg, static

	length mm	24h EC50 mg/l
Annelida:		
Lepidonotus squamatus	15	>6400
Polydora sp.		>6400
Crustacea:		
Balanus crenatus (Rock barnacle)	6	>6400
Eupagurus bernhardus (Hermit crab)	11.4	>6400
Carcinus maenas (shore or green crab)	12.6	>6400
Mollusca:		
Lepidochitona cinerea (Chiton)	6.5	>800
Acmaea testudinalis (Limpet)	2.5	>6400
Aphorrhais pes-pelicani (Pelican's foot)	43	>3200
Thais (Nucella) lapillus (Dow whelk)	15	>6400
Buccinum undatum (Large whelk)	31	>6400
Onchidoris fusca (Sea slug)	13	>6400
Mytilus edulis (Common bay mussel)	28	>6400
Anomia ephippium (False saddle oyster)	6.5	>6400
Hiatella (Saxicava) arctica (Red nose)	23	>1600
Echinodermata:		
Asterias rubens (Starfish)	59	>6400
Psammechinus miliaris (Sea urchin)	31	>6400
Urochordata:		
Ascidiella scabra (Sea squirt)		>6400

17-OCT-2001 (82)

Memo: TOXICITY TO INVERTEBRATES

Remark: Toxicity of sodium sulfate in vitro on the fish nematode Procamallanus sp. was examined. Complete mortality was observed after 48 hours with 0.5% solution, and after 20 hours in 1.0% solution.

11-JUL-2003 (61)

Memo: TOXICITY TO INVERTEBRATES

26-SEP-2005 (5)

Memo: TOXICITY TO MICROORGANISMS

Remark: Stimulation of growth (117 - 120 %) of Spruce seedlings was observed after addition of sodium sulfate (84 mg NaSO4 added to vessel of 110x230 mm with 150 mm soil layer) to soil, due to activation of soil microflora. The total test period was 107 days.

15-OCT-2001 (64)

Memo: TOXICITY TO PLANTS

Remark: 48 hours test with bulbs/seeds in a liquid test medium and with Na2SO4 in a semi-static test. Test parameter root length.

Allium cepa, bulbs (Modified Allium test) : 7756 mg/l IC50
Lepidium sativum, seeds (Lepidium test): 8533 mg/l IC50

15-OCT-2001 (8)

Memo: TOXICITY TO PLANTS

Remark: Method: greenhouse equipped with an activated charcoal air filtration system,
22 degree C day/18 degree C night, 50-55 % rel. air humidity, 12h photoperiod,
treatment 3 x/week:
0.5, 1, 3, 5 g Na2SO4 as dust / 6 moistened plants
Pinto-beans, 28d old
"Veemore" tomatoes, 35d old
Results:
Pinto-beans; Progressive decrease in growth and dry weight with increasing Na2SO4 conc. over 4w
"Veemore" tomatoes;
1w with 3 and 5 g/l or 2w with 1 g/l : growth inhibition
3w with 0.5 g/l : no inhibition

15-OCT-2001 (93)

Memo: TOXICITY TO PLANTS

Remark: Effect of Na2SO4 on the symbiotic effectiveness of the host Vigna radiata (mungo bean) and Rhizobium, 30 d:
Initiation of nodulation was delayed by one day at 0.05 %;
Total number of nodules and total nitrogen content of plant was maximum at 0.05 %;
Nodulation was caused only upto 0.3 %.
Method: Test tube method acc. to:
Vincent, J.M.: Manual for the practical study of root nodule

bacteria, Blackwell Scientific Publications, Oxford (1970)

24-OCT-2001 (10)

Memo: TOXICTY TO AQUATIC PLANTS / INVERTEBRATES

Remark: Na2SO4, dissolved in tap water, neutralized with Ca(OH)2:

Hydra oligactis (Coelenterata):
disintegration in 0.5% within 20-36h
Turbellaria:
Planaria gonocephala: death and disintegration in 1% after 48 h
Stenostomum: death and disintegration in 0.5% after 24h
Mollusca:
Limnaea stagnalis
Planorbis carinata in 1.5% after 24h dead, in 1% within
Valvata piscinalis 3-14d dead
Bythinia tentaculata
Crustacea:
Daphnia hyalina 0.25% lethal
Insects:
Limnophilus (Caddisfly,larvae): in 0.5% within 15-19d dead, in 1 und 1.5% within 4d dead
Fishes:
Carassius vulgaris (Gold fish): 0.5-1.25% no effect;
1.5% within 24d dead;
2% within 7-8d dead
Tinca vulgaris (Tench) : 0.5% no effect;
1% within 21d dead;
2% within 1-2d dead
Perca fluviatilis (Perch) : 0.5% no effect;
in 2% within 2-7d dead
Alburnus bipunctatus (Bleak) : in 1% within 16-17d dead
Scardinius erythrophtalmus
(Rudd) : in 1.5% within 7d dead
Squalis leuciscus (Chub) : in 2% within 2d dead
Salmo fario and : in 1.5% after 48h dead;
Salmo gairdneri (Trout) 15-20 cm in 2% after 36h dead
Tadpoles in 2% after 3.25-9h dead;
in 1.1 % after 6h dead
Submerse plants:
Potamogeton luceus (pondweed):
in 1.5 and 2% within 26d disintegration
Ceratophyllum demersum (horn wort):
in 0.3% no damage;
in 1.5% within 40d disintegration
Myriophyllum verticillatum (milfoil):
in 1.5% within 12d dead;
in 1% within 40d disintegration
Elodea canadensis (pondweed):
in 0.1% no damage;
in 0.25% within 18d disintegration
Lemna minor (duckweed):
in 1% after 30d end of leaf reproduction;
in 0.5% no damage
Callitriche: in 0.8% permanent damage and deformation;
in 1% dead
Fontinalis : in 0.8% within 25d no damage;
in 1.5% dead and disintegrated
Chara foetida (filamentous green alga):
in 0.5 and 0.75% up to 60d increased growth;

within 72d dead

26-SEP-2005 (86)

09-NOV-2001

5.0 Toxicokinetics, Metabolism and Distribution

In Vitro/in vivo:	In vivo
Type:	Absorption
Species:	other: homo sapiens
No. of animals, males:	7
No. of animals, females:	0
Doses, males:	13.9 g (8.6 g of the anhydrous salt)
Route of administration:	oral unspecified
Exposure time:	3 hour(s)

Year:	1983
GLP:	no
Test substance:	other TS: Mg2SO4

Remark: Conclusion: Magnesium sulfate is less completely absorbed than sodium sulfate as described by Cocchetto et al, 1981

Result: prior to study, three consecutive 24-hour periods for urine volume determination (twice, one -week interval). Subjects received either above dose in four hourly increments or just water; one week later the alternative.
72 -hour urine was collected at 4-hourly intervals (8 at night) Urinary sulfate excretion corrected for baselien was about 30.2% +- 17.2 in the first 24 hours, negligible in the following 48 hours. All subjects given the sulfate had gastro-intestinal complaints and loose stools or diarrhea.

Test condition: Frequency of treatment: once
Post exposure period: 72 hours
Control group: No; subject as own control

Reliability: (2) valid with restrictions
non-standard study

26-SEP-2005 (70)

In Vitro/in vivo:	In vivo
Type:	Distribution
Species:	other: homo sapiens
No. of animals, males:	8
No. of animals, females:	0
Doses, males:	60-80 microCurie
Route of administration:	other: intravenously and oral

Year:	1976
GLP:	no
Test substance:	other TS: Na2SO4 (35S-labeled)

Result: Volunteers received above dose IV, followed by 24-hours fluid restriction and blood and urine collection to determine radio-activity and creatinine concentration
Same volunteers received same amount orally 14 days later, followed by same regimen.
Plasma equilibrium iwas reached within 90 and 105 minutes respectively.
Calculated mean extracelluar fluid space was 16.8 +- 1.1 and 15.3 +- 1.2 respectively or only 9%.
Conclusion: 35S-labeled sulfate is absorbed completely and rapidly.

Test condition: Exposure period: single dose I.Vl, single dose oral 14 days later
Frequency of treatment: once daily
Post exposure period: 24 hours
Control group: No; subject as own control

Reliability: (2) valid with restrictions
non-standard study
(12)

In Vitro/in vivo:	In vivo
Type:	Absorption
Species:	other: homo sapiens
No. of animals, males:	5
No. of animals, females:	0
Doses, males:	18.1 g Na2SO4 decahydrate (800 g of the anhydrous salt)
Route of administration:	oral unspecified

Year: 1981
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Conclusion: Sodium sulfate is better absorbed from the intestine when given in divided dose than from a single large dose, indicating saturation of the transport system.

Result: Prior to exposure three separate 24-hour periods for urine volume and baseline sulfate excretion determination (twice, one -week interval). Subjects received either above dose in a single dose or in four hourly increments; one week later the alternative dosing schedule.
72 -hour urine was collected in 24-hour portions. Urinary free sulfate excretion corrected for baseline was about 53.4 +-16.8 for the single dose and 61.8 +-7.8 for the divided dose. Single dose causeds severe diarrhoea, divided dose did not. Excretion of free sulfate is not influenced by urine flow, but excretion of organicaly bound sulfate is.in a linear fashion.

Test condition: Exposure period: single oral dose or divided over three hours
Frequency of treatment: twice with one week interval
Post exposure period: 72 hours
Control group: No; subject as own control

Reliability: (2) valid with restrictions
non-standard study

26-SEP-2005 (27)

Type: Absorption
Species: rat

26-SEP-2005

Result: Absorption of inorganic sulfate after ingestion in rats (male, Wistar (30-330 g body weight) was investigated. A

inorganic sulfate concentration was measured in the serum after 2 hours of oral administration of 5 mmol Na2SO4. A threefold increase in serum sulfate concentration was measured. Compete absorption from the gastrointestinal tract was measured using 35S labelled sulfate.

Reliability: (2) valid with restrictions
non-standard study

26-SEP-2005 (60)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50
Species:	rat
No. of Animals:	10
Vehicle:	water
Doses:	2-5 ml/100 g body weight oral
Value:	> 10000 mg/kg bw
Method:	other: not defined
Year:	1971
GLP:	no data
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED: not described STATISTICAL METHODS: not described METHOD OF CALCULATION: not described
Result:	MORTALITY: - Time of death: after 8 days - Number of deaths at each dose: not described CLINICAL SIGNS: no clinical signs observed NECROPSY FINDINGS: not described POTENTIAL TARGET ORGANS: not described SEX-SPECIFIC DIFFERENCES: not described
Test condition:	TEST ORGANISMS: - Source: not described - Age: not described - Weight at study initiation: mean weight 270 gram - Controls: not described ADMINISTRATION: - Doses: as described - Doses per time period: not described - Volume administered or concentration: 2-5 ml - Post dose observation period: 8 days EXAMINATIONS: not described
Reliability:	(4) not assignable Original reference not available

27-SEP-2005 (52)

Type:	LD50
Species:	mouse
Value:	= 5989 mg/kg bw
Year:	1963
GLP:	no data
Test substance:	as prescribed by 1.1 - 1.4
Reliability:	(4) not assignable Original reference in Japanese not available

27-SEP-2005 (78)

Type:	other: human drinking-water study
Species:	human
Sex:	male/female
No. of Animals:	10
Vehicle:	water
Doses:	dose ranging study: 0, 400, 600, 800, 1000 and 1200 mg/l.

Single dose study: 0 and 1200 mg/l.

Method: other
Year: 1997
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS: 10 Normal Human Subjects, 80% caucasian.
- Source: -
- Age: 24-45 years
- Weight at study initiation: -
- Controls: -
ADMINISTRATION:
- Doses: dose ranging study: 0, 400, 600, 800, 1000 and 1200 mg/l. Single dose study: 0 and 1200 mg/l.
- Doses per time period: dose ranging study: 4 subjects (2 male, 2 female) received a dialy dose in the order listed above for 6 consectutive 2 day periods. Single dose study: 6 subjects (3 male, 3 female) received a dialy dose of 0 and 1200 mg/l for 2 consecutive 6 day periods.
Colored markers were given at the beginning of each change in drinking water sulfate concentration.
- Volume administered or concentration: volume 36 ml/kg/d.
- Post dose observation period:
EXAMINATIONS: The health of the subjects was determined by studying their history, physical examination, urineanalysis, blood cell counts and serum chemistries. During the study stool mass, frequency and consistency in mouth to anus appearance of colored markers were measured.

Wilcoxon signed rank test was used to compare the effects of specific concentrations of sulfate compared to distilled water.

Result: MORTALITY: -
- Time of death: -
- Number of deaths at each dose: -
CLINICAL SIGNS: No significant change in bodyweight. All blood and urine test results were normal. At 1200 mg/l 8 subjects rated the taste of the water as neutral-slightly unpleasant, 1 subject as moderately unpleasant and 1 subject as very unpleasant.

Dose ranging study:
Increasing the sulfate concentration in drinking water every 48 hours from 0 - 1200 mg/l produced no significant trend in stool mass per hours (based on Page's L-statistic test). During the six periods the mean number of stools were 2.5, 3.0, 2.3, 3.0 2.0 and 2.8 respectively, and the mean consistency ratings were 3.5, 3.3, 3.1, 3.4, 3.0 and 2.7 respectively. There was a significant trend toward decreasing mouth to anus appearance time with increasing sulfate concentration. The mean appearance times were (hours) 27.3, 17.9, 26.0, 16.1, 19.2, 17.2 respectively. No diarrhea during daily diaries were reported during the entire study. Mild abdominal cramps were reported by one subject for two days while receiving distilled water.

Single dose study:
Compared to distilled water, water containing 1200 mg/l sulfate produced a statistically significant increase in the

mean stool mass per six-day pool, from 629 to 922 g and in mean stool mass per hour from 4.8 to 6.6 g. Each subject showed an increase in stool mass per pool and in stool mass per hour. Stool frequencey, stool consistency, and mouth to anus appearance time were not significantly different. Two of the six subjects reported abdominal cramps, no other symptoms were recorded.

When combing the results from both studies for 0 an 1200 mg/l significant decreases in stool consistency and appearance time were noted at 1200 mg/l.
NECROPSY FINDINGS: -
POTENTIAL TARGET ORGANS: -
SEX-SPECIFIC DIFFERENCES: -

Test substance: Anhydrous sodium sulfate from UPS was used.
Reliability: (2) valid with restrictions
Acceptable, well documented study.
The results of the blood and urine test an bodyweights are not shown.

27-SEP-2005 (51)

5.1.2 Acute Inhalation Toxicity

Type:	LCLo
Species:	rat
Strain:	Sprague-Dawley
Sex:	male
No. of Animals:	6
Vehicle:	water
Doses:	10 mg/m3
Exposure time:	72 hour(s)
Value:	> 10 mg/m³
Method:	other: see freetext, not a guideline study: method according to Last and Cross, J. Lab. Clin. Med. 91:328-339 (1978)
Year:	1980
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: rats were exposed to well characterized aerosols of sodium sulfate at levels of 10 mg/m3 and particle sizes of around 1 micron. the responses to breathing these aerosols for three days were evaluated by measurements of glycoprotein, RNA and DNA contents of homogenates of the lungs and quantification of wet to dry weight ratios of the lung lobs.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described
ANALYTICAL METHODS: Ion chromatography as described by Asgupta et al., Amer. Ind.Hyg. Assn. J. (1980) in prep.
Result: MORTALITY: no death reported
CLINICAL SIGNS: RNA, DNA and protein levels in lung homogenates (control = 100)
RNA: 99, DNA: 100, protein content: 107. (mean values form 6 rats)
NECROPSY FINDINGS: Lung wet to dry ratio: (control = 4.5). 4.35 and 4.5 for exp. 1 and 2 resp.
POTENTIAL TARGET ORGANS: Lungs
SEX-SPECIFIC DIFFERENCES: not determined
Test condition: TEST ORGANISMS: rat

- Source: Charles River, Portage, MI, USA
- Age: 70-80 days
- Weight at study initiation: not described
- Number of animals: 6 rats per exposure
- Controls: yes
ADMINISTRATION:
- Type of exposure: inhalation
- Concentrations: 10 mg/m3
- Particle size: app. 1 µm
- Type or preparation of particles: Babington (1-15 mg/m3) and Retec nebulizers (> 0.1 mg/m3)
EXAMINATIONS: Lungs: RNA, DNA, protein from homogenates. Quantification of wet to dry weight ratios of right apical lung lobs.

Reliability: (2) valid with restrictions
Acceptable, well documented study.

27-SEP-2005 (62)

Type: other: effect on pulmonary function
Species: human
Vehicle: other
Doses: 1, 2 and 3 mg/m3
Exposure time: 10 minute(s)

Method: other: unspecified
Year: 1979
GLP: no
Test substance: no data

Method: TEST ORGANISMS: human
- Source: -
- Age: -
- Weight at study initiation: -
- Number of animals: 5 astmatic and 5 normal humans and 6 astmatic and 6 normal humans
- Controls: -
ADMINISTRATION:
- Type of exposure: aerosols
- Concentrations: 1, 2, 3 mg/m3 and 3 mg/m3 in the second experiment
- Particle size: 0.5 micrometer mass mediam aerodynamic diameter
- Type or preparation of particles: particles were generated by an ultrasonic nebulizer and sized by elctron micrographs and an electrical aerosol size analyzer.
EXAMINATIONS:
Respiratory resistance (Rrs) was meaured continuesly during exposure. Rrs, Forced Expiratory Volume1 and VC were measured 5, 15, 30, 45 and 60 minutes after exposure. In the second experiment lung volumes by spirometer and plethysmography, dynamic mechanisms of breathing by Rrs: specified airway conductance and flow volume curve, distribution of ventilation by single and multiple breath nitrogen washouts, random noise oscillations and diffuse capacity.

Result: MORTALITY:
- Time of death: -
- Number of deaths at each dose: -
CLINICAL SIGNS:
In the first experiment 2 of 5 astmatic people experienced a

15-20% fall in FEV1 at 1 mg/m3. This did not get worse at higher concentrations. The groups means were not altered as comapred with NaCl. In the second experiment no adverse effect on pulmonary function was found over 3 hours compared to NaCl. 2 of 6 astmatic people experienced a 15-20% fall in FEV1 at 1 mg/m3 after breathing NaCl and sodium sulfate aerosols.
NECROPSY FINDINGS: -
POTENTIAL TARGET ORGANS: -
SEX-SPECIFIC DIFFERENCES: -

Test substance: No data on sodium sulfate supplier, purity or storage.

Reliability: (4) not assignable
Not assignable. Only abstract available.

26-SEP-2005 (84)

Type: other: irritant potency (mucociliary clearance)
Species: rabbit
Strain: other: mixed breed
Sex: male
No. of Animals: 5
Doses: 1800-1950 microgram particles/m3
Exposure time: 1 hour(s)

Method: other
Year: 1984
GLP: no
Test substance: no data

Method: TEST ORGANISMS: Mixed breed rabbits.
- Source: -
- Age: -
- Weight at study initiation: 2.5-2.7 kg
- Number of animals: 5 males
- Controls: animals served as their own controls in 'sham'-control experiments. 10 of these experiments were performed exposing the animals for 1 hour to temperature and humidity conditioned air.
ADMINISTRATION:
- Type of exposure: inhalation.
- Concentrations: 1800-1950 microgram particles/m3.
- Particle size: mean mass aerodynamic diameter 0.4 micrometer.
- Type or preparation of particles: Aerosols were prpared by nebulization using a Laskin nebulizer. The aerosols were mixed with filtered room air which had been temperature and humidity conditioned.
EXAMINATIONS: The bronchial mucociliary clearance was measured by brief inhalation of radiolabelled, insoluble tracer microspheres (99mTc-tagged ferric oxide). The thoracic retention was measured externally in vivo. These measuerments began within 2 min. After the inhalation and were repeated after 24 hours to determine a value for residual activity (R24). It is expected that the tracer is completely cleared after 24 hours. The mucociliary clearance was determined as mean residence time (MRT) of the tracer.

Result: MORTALITY: -
- Time of death: -
- Number of deaths at each dose: -
CLINICAL SIGNS: No effect on mucociliary clearence was found (one way ANOVA, two tailed).

NECROPSY FINDINGS: -
POTENTIAL TARGET ORGANS: -
SEX-SPECIFIC DIFFERENCES:-

Test substance: No details on where the sodium sulfate was obtained or on purity are given.

Reliability: (2) valid with restrictions
Limited documentation but sufficient for assessment of primary effects.

27-SEP-2005 (87)

Type: other: irritant potency
Species: guinea pig
Strain: other: random bred
Sex: no data
No. of Animals: 10
Vehicle: no data
Doses: 0.90 +/- 0.11 mg/m3
Exposure time: 1 hour(s)

Method: other
Year: 1978
GLP: no
Test substance: no data

Method: TEST ORGANISMS: guinea pigs
- Source: -
- Age: -
- Weight at study initiation: 200-300 g
- Number of animals: 10
- Controls: during a 30 min. control period before exposure to the test substance measurements were taken every 5 min. The same animals were used in the exposure.
ADMINISTRATION:
- Type of exposure: inhalation.
- Concentrations: 0.90 +/- 0.11 mg/m3
- Particle size: 0.11 micrometer
- Type or preparation of particles: aerosols were prepared witha Dautrebande D30 aerosol generator.
EXAMINATIONS:
The respiratory meachanisms of the guinea pigs were measured. Intrapleural pressure, tidal volume, and rate flow of gas in and out of the respiratory system are recorded. From these data the pulmonary flow resistance may be obtained. Pulmonary flow resistance and the compliance are in cm water/ml/s and mm/cm water, respectively.

Result: MORTALITY: -
- Time of death: -
- Number of deaths at each dose: -
CLINICAL SIGNS: Pulmonary resistance and compliance of sodium sulphate was not significantly different from the control.
NECROPSY FINDINGS: -
POTENTIAL TARGET ORGANS: -
SEX-SPECIFIC DIFFERENCES: -

Test substance: No details on where the sodium sulfate was obtained or on purity are given.

Reliability: (4) not assignable
Documentation insufficient for assessment

27-SEP-2005 (4)

5.1.3 Acute Dermal Toxicity

5.1.4 Acute Toxicity, other Routes

Type:	LD50
Species:	rat
Route of admin.:	i.p.
Value:	3000 - 4100 mg/kg bw

Reliability:	(4) not assignable
	Reference not translated
26-SEP-2005	(20)

Type:	LD50
Species:	mouse
Route of admin.:	i.p.
Value:	2400 - 3400 mg/kg bw

Reliability:	(4) not assignable
	Reference not translated
26-SEP-2005	(20)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species:	rabbit
Concentration:	500 mg
Exposure:	Occlusive
Exposure Time:	4 hour(s)
No. of Animals:	3
Vehicle:	other: polyetyleneglycol 400
Result:	not irritating
EC classificat.:	not irritating

Method:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year:	1991
GLP:	yes
Test substance:	as prescribed by 1.1 - 1.4

Method:	METHOD FOLLOWED: Determination of irritant/corrosive effects were examined using rabbits, according to OECD 404. DEVIATIONS FROM GUIDELINE: no deviations reported GLP: yes STATISTICAL METHODS: DRAIZE score system was used METHOD OF CALCULATION: not described ANALYTICAL METHODS: not applied
Result:	AVERAGE SCORE - Erythema: score = 0, after 14 days - Edema: score = 0 after 14 days REVERSIBILITY: not described OTHER EFFECTS: Irrit. index : edema = 0.0; erytheme = 0.0. Body weight, 3.7 - 4.2 kg
Test condition:	TEST ANIMALS: Rabbits - Strain: HC:NZW - Sex: not described - Source: Interfauna, Ltd, UK

- Age: adults
- Weight at study initiation: not described
- Number of animals: 3
- Controls: Contralateral skin area not treated
ADMINISTRATION/EXPOSURE
- Preparation of test substance: 500 mg pulverized in PEG 400
- Area of exposure: dorso-lateral areas of the trunk.
- Occlusion: Patches hypoallergenic Hansamed (Beiersdorf)
- Vehicle: PEG 400
- Concentration in vehicle: 500 mg
- Total volume applied: not described
- Postexposure period: 14 days
- Removal of test substance: washed with water
EXAMINATIONS
- Scoring system: DRAIZE scores
- Examination time points: 1, 24, 48, 72 hours, 7, 14 days.

Reliability: (1) valid without restriction
Guideline study

26-SEP-2005 (13)

5.2.2 Eye Irritation

Species:	rabbit
Concentration:	90 mg
Dose:	100 other: µl
Exposure Time:	24 hour(s)
No. of Animals:	3
Vehicle:	no data
Result:	slightly irritating
EC classificat.:	irritating
Method:	Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"
Year:	1991
GLP:	yes
Test substance:	as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Determination of irritant/corrosive effects were examined using rabbits, according to OECD 405.
DEVIATIONS FROM GUIDELINE: no deviations reported
GLP: yes
STATISTICAL METHODS: DRAIZE score system was used
METHOD OF CALCULATION: not described
ANALYTICAL METHODS: not applied

Result: AVERAGE SCORE
- Cornea: 0 no effect (7 days), irrit. index 0.0
- Iris: 0 no effect (7 days) irrit. index 0.0
- Conjuntivae (Redness): 1 (48 hours) irrit. index 1.0
- Conjuntivae (Chemosis): 0 (7 days)
- Overall irritation score: 1.3 (slightly irritating)

DESCRIPTION OF LESIONS: no

REVERSIBILITY: within 7 days

OTHER EFFECTS: -

Test condition: TEST ANIMALS: Rabbits
- Strain: HC:NZW
- Sex: not described
- Source: Interfauna, Ltd, UK

- Age: adults
- Weight at study initiation: not described
- Number of animals: 3
- Controls: other eye

ADMINISTRATION/EXPOSURE
- Preparation of test substance: Pulverized powder
- Amount of substance instilled: 90 mg
- Vehicle: not described
- Postexposure period: 21 days
- exposure : 24 hours

EXAMINATIONS
- Ophtalmoscopic examination: yes
- Scoring system: DRAIZE system
- Observation period: 21 days
- Tool used to assess score: optical instrument (hand slit lamp)

Reliability: (1) valid without restriction
Guideline study

26-SEP-2005 (13)

5.3 Sensitization

Type:	Patch-Test		
Species:	human		
Concentration 1st:	Induction	1.25 %	semiocclusive
2nd:	Challenge	1.25 %	semiocclusive
No. of Animals:	65		
Vehicle:	water		
Result:	not sensitizing		
Classification:	not sensitizing		

Method: other: not specified
Year: 1976
GLP: no
Test substance: other TS

Method: TEST ANIMALS: human
- Strain: -
- Sex: male/female
- Source: -
- Age: 16-70
- Weight at study initiation: -
- Number of animals: 56 male and 5 female
- Controls: -

ADMINISTRATION/EXPOSURE
- Study type: Patch test.
- Preparation of test substance for induction: A 1.25% aqueous solution was prepared. This concentration represents a 100 fold increase of the normal use level.
- Induction schedule: Subjects were exposed on their backs. The test patch unit consited of a strip of two-inch wide blenderm surgical tape with two rows of five 12.7 mm filter paper discs each. The first application lasted for 48 hours. All other inductions were for 24 hours. Reactions tohe initial site were scored 48 and 96 hours after patch removal. 8 other 24 hour inductions were done on mondays, Wednesdays and Fridays (3.5 weeks)on 3 alternate sites (unless the reaction or tape irritation was severe than

other sites were used). Reactions were recorded 3-9 hours before application and 24 hours after patch removal.
- Concentrations used for induction: 1.25% aqueous solution.

- Concentration in Freuds Complete Adjuvant (FCA): -
- Challenge schedule: On monday in week 7 subjects were challenged on a previously unpatched site. After 48 hours the patches were removed. The patches were scored 48 hours 48 following removal.
- Concentrations used for challenge: 1.25% aqueous solution.

- Rechallenge: subjects that showed signs of sentisation in the challenge phase were tested again after a 2 week rest period.
At the original concentration under occlusion, in a dilution of original strenght (1:3) under occlusion, as used in practice (subject applied the project to the flex part of the arm 3 times/day for 5 days.
- Positive control: -
EXAMINATIONS
- Grading system: patch reactions were scored by experienced technitians. According to teh following scoring system:
0 No evidence of any effect
+/- Barely perceptible. Minimal faint unifrom spotty erythema.
1 Mild. Pink unifrom erythema covering most of the contact site.
2 Moderate. Pink-red erythema visibly uniform in the whole contact site.
3 Marked. Bright red erythrema with accompanying edema, petechiae or papules.
4 Severe. Deep red erythema with vesiculation or weeping with or without edema.
- Pilot study: -

Result: RESULTS OF PILOT STUDY: -

RESULTS OF TEST
- Sensitization reaction: One subject showed a score 1 reaction during the induction period. Other subjects did not react to the application (data not shown).
- Clinical signs: Mild. Pink unifrom erythema covering most of the contact site.
- Rechallenge: Data not shown.

Test substance: Bath salt crystals allegedly containing 80.8% sodium sulfate.

Reliability: (4) not assignable
The report is incomplete and unsigned. Lab and authors are unknown and there is no quality control. Individual data are not shown.

26-SEP-2005 (22)

5.4 Repeated Dose Toxicity

Type:	Sub-acute	
Species:	rat	Sex: male
Strain:	Sprague-Dawley	
Route of administration:	oral feed	
Exposure period:	4 weeks	
Frequency of treatment:	diets were provided ad libitum for 4 weeks	

Post exposure period: none
Doses: Experiment a 0.88 mmol/kg feed
Experiment b 8.64 mmol/kg feed day 1-8
17.28 mmol/kg feed day 9-16
34.56 mmol/kg feed day 17-24
65.12 mmol/kg feed day 25 for 4-6 days
Experiment c 138 mmol/kg feed
Control Group: yes, concurrent no treatment
NOAEL: ca. 2000 mg/kg

Method: other: not specified
Year: 1960
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS: Sprague Dawley rats
- Age: weanling, young
- Weight at study initiation:
- Number of animals: 6 rats per group
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 4 weeks
- Type of exposure: oral feed, diet avaialable ad libitum
- Post exposure period: none
- Vehicle: basal diet, cornstarch diet, 67% cornstarch, 24% 'vitamin free' casein, 5% crisco (cristalized cottonseed oil) and 4% salt mixture (3.8% magnesium sulfate, anhydrous and 0.02% maganous sulfate. No sodium sulfate.) and vitamins.
- Concentration in vehicle: see doses
- Total volume applied: the feed intake in week 4 of the rats receiving sodium sulfate is presented: 408 (371-453) g.

- Doses:
Experiment a 0.88 mmol/kg feed
Experiment b 8.64 mmol/kg feed day 1-8
17.28 mmol/kg feed day 9-16
34.56 mmol/kg feed day 17-24
65.12 mmol/kg feed day 25 for 4-6 days
Experiment c 138 mmol/kg feed
SATELLITE GROUPS AND REASONS THEY WERE ADDED: -
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: records of any diarrhea that occurred were kept. In experiment c teeth were examined.
- Mortality: -
- Body weight: at the beginning of the study, at the end of each week and just before study termination.
- Food consumption: feed intakes and feed:gain ratios were obtained for each week.
- Water consumption: In experiment c the amount of water drunk during the first 48 h of the third week was recorded.
- Ophthalmoscopic examination: -
- Haematology: In experiment c blood was colelcted from the tail after 3.5 weeks for red and white bloodcell counts and hemoglobin was determined. At termination of the study bllod was collected from the neck vain and analyzed for alkaline phosphate, inorganic phosphate and protein.
- Biochemistry: -
- Urinalysis: In experiment c the volume of urine was determined.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: gastrointestinal organs were examined. The

small intestine and colon plus rectum were hung full length were measured. Organs were clenaed dried and weighed. I
- Microscopic: In experiment c a small snip of the stomach was removed for histological examination.
OTHER EXAMINATIONS: -
STATISTICAL METHODS:
In experments b and c the numerical results were analyzed statistically by analysis of variance, the hypothesis in every case being that the groups were equal. A multiple range test was performed when it was indicated that there was a difference among the groups at the 5% level or less. results were significantly different if P<0.05.

Result: NOAEL (NOEL), LOAEL (LOEL): At the top dose, the food contained around 2% of the respective sulfates, calculated to be around 2000 mg/kg/d.
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX:
- Time of death: -
- Number of deaths at each dose: 0
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
Data for experiment a are not presented in the article because at this low dose level no effects were seen.
- Mortality and time to death: -
- Clinical signs: Experiment c teeth: no changes compared with control group. Two slight cases of diarrhea that lasted for a day were observed in experiment b in the sodium sulfate group. One rat in experiment c showed diarrhea on 4 different days (3 conseccutive days) in the middle of the feeding period.
- Body weight gain: Experiment b and c: no changes compared with control group.
- Food/water consumption: Experiment c: no changes compared with control group.
- Ophthalmoscopic examination: -
- Clinical chemistry: -
- Haematology: Experiment c: no changes compared with control groups or other dose groups In red or white blood cell counts, hemoglobin, protein, alkaline phosphatase orminorganic phosphatase.
- Urinalysis: Experiment c urine volume: no changes compared with control groups or other dose groups.
- Organ weights: Experiment b and c: no changes compared with control group.
- Gross pathology: -
- Histopathology: -
- Other: -
STATISTICAL RESULTS: see above

Test substance: Sodium Sulfate was obatined as anhydrous powder from Merck, A.C.S.

Reliability: (2) valid with restrictions
Old study non-GLP and not according to standard guideline.

26-SEP-2005 (68)

Species:	rat	Sex: male
Strain:	no data	
Route of administration:	inhalation	
Exposure period:	8, 12, 44, 90, 720 hrs	
Frequency of treatment:	continuous (?)	
Post exposure period:	1 month (size of recovery group not given)	
Doses:	3, 11.06, 18.03, 40.05, 60.45 mg respectively, with concurrent exposure to 500 mg/l in drinking water	
Control Group:	other: one control group for each exposure group, size	

not specified

Year: 1989
GLP: no

Remark: ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX:
cannot be calculated
Aerosol generation not described. Aerosol size, stability not described. exposure duration / day not given
Concentrations measured by potentiometric method
Calculated daily dose from inhalation at 3 mg/m3 is 0.66 (8 hr/day) to 2 mg/kg/day (24hr/day), compared to intake from drinking water 60 mg/kg/day.
LOAEC: 2 mg/m3
log(time-to-first appearance) plotted against log(concentration) shows 100% linear correlation for 2 of the 3 reported effect parameters. Such precision is unlikely to occur in biological systems.
Number of animals: 200; 5 exposure groups and 5 control groups, size not given. Report mentions complete recovery at 1 month post-exposure but size of recovery group not given. method for monthly isnpections of inner organs not given.
Time of death: n/a
Nr. of of deaths at each dose: none
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality and time to death: n/a
Clinical signs: not specifed

Result: At concentrations of 60, 40, 16, 11 and 3 mg/m3:
small but statistically significant effects on serum liver cholinesterase concentration (first appearing at 6, 12, 44, 90 and 720 hours respectively), prolongation of blood coagulation time (first appearing at 4, 8, 30, 64 and 510 hours respectivey) and brain irritablity as measured by "summated threshold potential (?)", (first appearing at 4, 8, 24, 45 and 288 hours respectively),
effects stated to be worse at end-of exposure (no data provided). Depression of spermatogenesis (presumably at end-of-exposure), at al concentrations.
All effects stated to be completely reversible within one month post-exposure (size of recovery groups not given).
Body weight gain:
- Food/water consumption: drinking water contained 500 mg sodium sulfate/liter. Consumptio data not given -
Ophthalmoscopic examination:
- Clinical chemistry: no abnormalities in blood histamine, brain cholinesterase, number of sulfhydryl groups,basic phosphatase activity in blood serum and content of ascorbic acid in the adrenals.
- Haematology:
No abnormalities were observed in number of erythrocytes and leucocytes, total haemoglobin, meth- and sulfhaemoglobin, presence of Heinz-Ehrlich bodies
- Urinalysis:
- Organ weights:
- Gross pathology:
- Histopathology: (? method not given) suppression of spermatogenesis
- Other:
STATISTICAL RESULTS: see above

Reliability: (3) invalid
results biologically implausible / insufficient

documentation for assessment

26-SEP-2005 (29)

Type: Chronic
Species: rat Sex: male
Strain: no data
Route of administration: inhalation
Exposure period: 3 months
Frequency of treatment: not given
Post exposure period: 1 month (size of recovery group not given)
Doses: dust concentration 1 mg/m3, with concurrent exposure to 500 mg/l in drinking water
Control Group: yes

Year: 1990
GLP: no

Remark: Dust generation, particle size, aerosol stability etc not described
exposure duration per day not given
Measured exposures in workplace atmosphere (shift average) 88 mg/m3, yet apparenty no clinical symptoms or complaints from humans
Method for "monthly ispection of inner organs" not given
Sulfate concentration in drinking water 500 mg/l;
caluculated maximum uptake from air < 0.1 (8-hr exposure) to .6 mg/kg/day (24hr/day exposure) vs. 60 mg/kg/day from drinking water

Result: small but significant changes in "summarized threshold potential" (measure of brain irritability), liver cholinesterase, blood cholinesterase, number of lymphocytes and neutrophils, body weight, relative liver weigt; depression of spermotagenesis, histopathological changes in liver and testes, serious histopathological changes in the lungs and several cases of pneumonomia, all fully reversible after 1 month recovery.
results similar to those found in concurrent studies with sodium sulfite at 01. and 1 mg/m3 and a mixture of sulfite/sulfate at 1 mg/m3.
Test substance: Na2SO4 dust, not specified
Reliability: (3) invalid
Results biologically implausible; insufficient documentation for assessment

26-SEP-2005 (30)

Species: rat Sex:
Route of administration: oral feed
Exposure period: 6 weeks
Frequency of treatment: daily (feeding study)
Doses: 1 or 2 % in diet
Control Group: other: saline in equal concentrations

Method: other: not described
Year: 1976
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: In two experiments the direct effect of dietary intake of sodium sulfate was examined. One experiment with weanling rats, and another with adults, over

a 6 weeks exposure period.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described

Result: NOAEL (NOEL), LOAEL (LOEL): not determined
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality and time to death: not described
- Clinical signs: not described
- Body weight gain: expl weanling rats upto 10 g S/kg dm and exp2 adult rats upto 20 g S/kg dm (exp1/exp2)
control expl : 4.54 g/d
control exp2 : -1.42 g/d
exp1 : 4.49 g/d
exp2 : -1.95 g/d
- Food/water consumption:
water:
control expl : 28.0 ml/d
control exp2 : 36.8 ml/d
exp1 : 36.2 ml/d
exp2 : 57.4 ml/d
food:
control expl : 13.4 g/d
control exp2 : 13.8 g/d
exp1 : 13.5 g/d
exp2 : 15.2 g/d
STATISTICAL RESULTS: not described, Overall dietary supplementation with sodium sulfate did not significantly affect food/water intake and live-weight gain of rats.

Test condition: TEST ORGANISMS
- Age: not described
- Weight at study initiation: not described
- Number of animals: eight weaning and eight adult animals
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 6 weeks
- Type of exposure: oral
- Post exposure period: not described
- Vehicle: commercial diet
- Concentration in vehicle: 10-20 gram S/kg dm
- Total volume applied: not described
- Doses: in daily diet
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: no
- Mortality: not described
- Body weight: yes
- Food consumption: yes
- Water consumption: yes
- Ophthalmoscopic examination: no
- Haematology: no
- Biochemistry: no
- Urinalysis: no
STATISTICAL METHODS: not described

Reliability: (3) invalid
documentation was insufficient for assessment

26-SEP-2005 (104)

Type:	Chronic	
Species:	hen	Sex: female
Strain:	other: White Leghorn	
Route of administration:	drinking water	
Exposure period:	3-4 weeks	
Frequency of treatment:	continuous	
Doses:	250-23328 mg/l	

Control Group: yes
LC100 : ca. 23328 mg/l

Method: other: not a guideline study, see freetext
Year: 1974
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Commercial strain hens were supplied with sodium sulfate containing drinking water for a period of 4 weeks. Egg production, body weight, water en feed consumption and mortality were examined.
STATISTICAL METHODS: performance of treatement were compared to performance during pretreatment.
METHOD OF CALCULATION: not described
ANALYTICAL METHODS: no

Result: NOAEL (NOEL), LOAEL (LOEL): not described
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality and time to death: at 16000 mg/l Na2SO4 cumulative death of 100% was observed at day 14, while death was already apparent at day 5.
- Clinical signs: not described

Conc. (mg/l Na2SO4)	egg production	water consumption	food consumtion	body weight
250	+6.5	-2.3	+13.3	+9.0
370	-16.1	-12.9	-3.7	-0.6
1000	+26.7	-2.0	+1.3	+1.3
1480	-15.6	-14.9	-1.7	+2.0
4000	+0.5	-12.0	+8.1	+1.1
5920	-24.4	+58.8	-14.2	-0.3
16000	-43.7	+146.7	-25.5	-14.7
23328	-73.8	-47.1	-77.8	*

* all animals died

- Ophthalmoscopic examination: -
- Clinical chemistry: -
- Haematology: -
- Urinalysis: -
- Organ weights: -
- Gross pathology: Necropsis of birds receiving 16000 mg/l sulphate showed extreme emaciation and visceral gouit.
- Histopathology: Microscopic examination of kidney tissues showed urate accumulation of individual glomeruli and tubules losing cellular detail.
- Other: none
STATISTICAL RESULTS: not described

Test condition: TEST ORGANISMS
- Age: not described
- Weight at study initiation: not described
- Number of animals: 2 hens per cage, 6 per block in 2 or 3 cage rows in
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 4 weeks with 4 weeks pretreatment
- Type of exposure: continuous in drinking water
- Post exposure period: no
- Vehicle: water
- Concentration in vehicle: 250, 1000, 4000 and 16000 mg/l

Na2SO4
- Total volume applied: n.a.
- Doses: not described
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: no
- Mortality: yes
- Body weight: yes
- Food consumption: yes
- Water consumption: yes
- Ophthalmoscopic examination: no
- Haematology: no
- Biochemistry: no
- Urinalysis: no
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: gout
- Microscopic: kidneys
OTHER EXAMINATIONS: egg production
STATISTICAL METHODS: all data were converted to performance percentages using the formula performance during treatment/performance during pretreatement x 100. Data were analyzed by analysis of variance when warranted.

Reliability: (2) valid with restrictions
No guideline study, but includes detailed information on used method, endpoints and statistical evaluation procedures.

07-AUG-2006 (1)

Type:	Sub-acute	
Species:	other: Cattle	Sex: male
Strain:	other: Holstein	
Route of administration:	oral feed	
Exposure period:	21 days	
Frequency of treatment:	ad lib	
Post exposure period:	not applicable	
Doses:	0.8% in diet	
Control Group:	yes	
LOAEL:	ca. .8 %	

Method:	other: non-protocol
Year:	1991
GLP:	no
Test substance:	other TS

Remark: only three controls, sulfur content of diet not reported. However, effects so serious that they can safely be assumed to be absent in any control population.

Result: In a study with 9 young Holstein steers (validity 3, controls insufficiently desribed), a concentrate diet containing 0.8 % sodium sulfate (total sulfur content appoximately 0.36%) was given during 21 days. 3 controls were given the same diet without added sodium sulfate (total sulfur or sulfate content not reported). Five out of nine test animals vs. no controls developed clinically manifest poli-encephalomalacia (PEM) as well as macroscopically visible and histologically recognisable cerebral lesions (brain histology of not-affected animals not reported) . The onset of the disease correlated well with increasing concentrations of sulfide in the rumen. Thiamine concentrations in serum (another alleged cause of PEM) were not significantly affected. Similar disease due to high sulfur content of food was allegedly also reported earlier

in sheep
Test substance: Test substance: dosing based on total sulfur content of feed, brought up to required level by adding sodium sulfate
Reliability: (2) valid with restrictions
26-SEP-2005 (45)

Type: Sub-acute
Species: other: cattle Sex: male
Route of administration: oral feed
Exposure period: 5 weeks
Frequency of treatment: ad lib
Post exposure period: not applicable

Doses: 3860 ppm; 5540 ppm; 7010 ppm
Control Group: no
LOAEL: ca. 3860 ppm

Method: other: non-protocol
Year: 2002
GLP: no
Test substance: other TS

Result: three groups of 5 young heifers / group were fed diets with 3860 ppm, 5540 ppm and 7010 ppm of sulfur respectively during 5 weeks. Sulfur concentrations were reached by adding sodium sulfate to the desired level. Microscopic signs of PEM were seen in all four low-dose animals, macroscopic signs in 4/5 medium-dose and 4/5 high-dose animals. Clinical signs of PEM were seen in all animals. Onset of PEM correlated highly with sulfide concentrations in rumen. Other potential causes of PEM were excluded. (Niles, 2002.)
Test substance: Test substance: dosing based on total sulfur content of feed, brought up to required level by adding sodium sulfate
Reliability: (2) valid with restrictions
No control group. Effects so serious that they can safely be assumed to be absent in any control population.
26-SEP-2005 (73)

Type: Chronic
Species: other: chicken Sex:
Strain: other: S.C.W.L.
Route of administration: oral feed
Exposure period: 11 days
Frequency of treatment: Daily (feeding study)
Doses: 1,2,3,4 or 5 % in diet
Control Group: yes

Method: other: no guideline study, see freetext
Year: 1976
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: The response of chicks of 14 days of age to increasing levels of dietary sodium sulfate were investigated. Weight gain and feed intake were observed.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described
Result: NOAEL (NOEL), LOAEL (LOEL): not determined
- Number of deaths at each dose: No death recorded
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL: yes
- Mortality and time to death: No mortality

- Clinical signs: not described
- Body weight gain: weight gain decreased with increasing sulfate concentration.
- Food/water consumption: not reported
STATISTICAL RESULTS: not described

Test condition: TEST ORGANISMS
- Age: 14 day-old male chicks
- Weight at study initiation: weight was main test parameter

- Number of animals: randomized block design with 60 treatments arranged as a 2x5x6 factorial, with two

replications.
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 11 days
- Type of exposure: oral
- Post exposure period: not described
- Vehicle: commercial diet (basal diet wth 18% crude protein)
- Concentration in vehicle: 0 - 5 gram sulfate per 100 gram food
- Total volume applied: water ad libitum
- Doses: in daily diet 30 diets in total
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: no
- Mortality: yes
- Body weight: yes
- Food consumption: yes
- Water consumption: not described
- Ophthalmoscopic examination: no
- Haematology: no
- Biochemistry: no
- Urinalysis: no
STATISTICAL METHODS: analysis of variance for determination of weight gain and gain:feed ration according to Snedecor, G.W. Statistical Methods, Coll. Press Ames, Iowa, USA (1956).

Reliability: (3) invalid
documentation was insufficient for assessment

26-SEP-2005 (91)

Species: pig Sex: no data
Route of administration: drinking water
Exposure period: 28 days
Frequency of treatment: daily
Doses: 54-1800 mg/l
Control Group: yes, concurrent vehicle

Method: other: see freetext
Year: 1992
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: The effect of sulfate in drinking water on nursery pig performance and health was examined over 28 days with 415 weaned pigs.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described

Result: NOAEL (NOEL), LOAEL (LOEL): not determined
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX
- Time of death: 1 pig died within the first week

- Number of deaths at each dose: 1 pig at 600 mg/l
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Clinical signs: Increased prevalence of diarrhea was a trend as sulfate concentration increased.
- Body weight gain: cumulative weight in kg of body-weight/kg (sd)

Week	Control	600 mg/l	1800 mg/l
1	0.79 (0.61)	0.94 (0.78)	0.80 (0.63)
2	2.56 (1.14)	2.78 (1.90)	2.4 (1.05)
3	4.30 (1.70)	5.05 (2.67)	4.49 (1.94)
4	6.53 (2.31)	7.59 (3.37)	7.16 (2.75)

Observations in week 4 were for both 600 and 1800 mg/l statistically significantly different

Increased
- Food/water consumption: A non-significant trend in increase water intake was observed with increasing sulfate concentration.No differences in feed intake were observed between various sulfate concentrations. Feed to gain ratios for all treatments were not different.

- Clinical chemistry: isolates of E-coli were found in 14% of the pigs, from 1 pig rotavirus was isolated. No pigs were exposed to transmissible gastroenteritis virus. None of the treatments had an adverse effect on nursery pig performance.

STATISTICAL RESULTS: not described separately

Test condition:
TEST ORGANISMS
- Age: 28 +/- 2 days
- Weight at study initiation: 6.8 kg mean weight
- Number of animals: 415 (male/female, males were castrated)
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 4 weeks
- Type of exposure: drinking water
- Post exposure period: not described
- Vehicle: farm well water
- Concentration in vehicle: 54, 600 and 1800 mg/l
- Doses: continuous in drinking water
- Feeding: pelleted 22% crude protein corn-soybean meal containing 20% dried whey. At the start of the third week the crude protein content was 18%.
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: Diarrhea, pathogenic E.coli and rota virus detection, enteropathogenicity in ligated intestinal loops, transmissable gastroentritus.
- Mortality: yes
- Body weight: yes, feed to gain ratio
- Food consumption: yes
- Water consumption: yes
- Ophthalmoscopic examination: no
- Haematology: yes
- Biochemistry: no
- Urinalysis: no
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: no

- Microscopic: no
OTHER EXAMINATIONS:
STATISTICAL METHODS: 7 replicates of 8 pigs/pen on water and 6 replicates of 8 pigs/pen for treatment with sulfate. Statistical evaluation compared mean water consumption, feed consumption, cumulative gain and feed-gain ratios by treatment group and week. Analysis of variance with repeated measures was used to account for the differences in treatment group over time. Initial weight was used as covariate in all analysis. Diarrhea scores were evaluated on an individual basis, using a non-parametric repeated measures design.

Reliability: (2) valid with restrictions
Acceptable, well documented publication which meets basic scientific principles.

26-SEP-2005 (108)

5.5 Genetic Toxicity 'in Vitro'

Type:	Ames test
System of testing:	S. Typhimurium TA1535, TA1537, TA100, TA98
Concentration:	312.5 to 5000 µg per plate with 4 dilutions
Cytotoxic Concentration:	no cytotoxicity observed
Metabolic activation:	with and without
Result:	negative

Method: other: Salmonella/Microsome test, Ames et al, Mutation Res. 31, 347-364 (1975)
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Ames test as described by Ames et al (1975). Test was performed in duplicate with varying concentration range.
DEVIATIONS FROM GUIDELINE: no guideline study
GLP: yes
STATISTICAL METHODS: not applicable
METHOD OF CALCULATION: not applicable
ANALYTICAL METHODS: not described

Result: EFFECTS:
- With metabolic activation: both tests, no effects
- Without metabolic activation: both tests, no effects
FREQUENCY OF EFFECTS: n.a.
PRECIPITATION CONCENTRATION: not described
MITOTIC INDEX: not described
CYTOTOXIC CONCENTRATION: no toxicity observed up to 5000 mg/l
TEST-SPECIFIC CONFOUNDING FACTORS: not described
STATISTICAL RESULTS: n.a.

Test condition: SYSTEM OF TESTING
- Species/cell type: Salmonella typhimurium LT2 mutants: TA 1535, TA 100, TA 1537, TA 98
- Deficiences/Proficiences: Histidine
- Metabolic activation system: LT2 system
- No. of metaphases analyzed: not described
ADMINISTRATION:
- Dosing: 4 concentrations, 312.5-625-1250-2500-5000 mg/l and 8-40-200-1000-5000 mg/l
- Number of replicates: 4 per test

- Application: plate
- Positive and negative control groups and treatment: pos. control: sodium azide, nitrofurantoin, 4-nitro-1,2-phenylene diamine and 2-aminoanthracene; negative control
- Pre-incubation time: not described
CRITERIA FOR EVALUATING RESULTS: Based on Maron and Ames (1983).

Reliability: (1) valid without restriction
Comparable to guideline study

26-SEP-2005 (13)

Type: Cytogenetic assay
System of testing: human blood lymphocytes
Concentration: 5*10e-5 to 5*10e-3 M
Cytotoxic Concentration: no data
Metabolic activation: no data
Result: negative

Method: other: not specified
Year: 1992
GLP: no
Test substance: no data

Method: SYSTEM OF TESTING
- Species/cell type: human lymphocytes
- Deficiences/Proficiences: -
- Metabolic activation system: -
- No. of metaphases analyzed: -
ADMINISTRATION:
- Dosing: -
- Number of replicates: -
- Application: -
- Positive and negative control groups and treatment: -
- Pre-incubation time: -
DESCRIPTION OF FOLLOW UP REPEAT STUDY: -
CRITERIA FOR EVALUATING RESULTS: -

Result: GENOTOXIC EFFECTS: -
- With metabolic activation: -
- Without metabolic activation: -
FREQUENCY OF EFFECTS: -
PRECIPITATION CONCENTRATION: -
MITOTIC INDEX: -
CYTOTOXIC CONCENTRATION: -
- With metabolic activation: -
- Without metabolic activation: -
TEST-SPECIFIC CONFOUNDING FACTORS: -
STATISTICAL RESULTS:
The frequency of chromosomal abberations, sister chromatid exchanges, and micronuclei was not increased in human blood lymphocytes in this experiment. Also there were no changes in mitotic index or lymphocyte cell cycle.

Test substance: No data on the test substance sodium sulfate.

Reliability: (4) not assignable
Not assignable. Results are given but this is just a statement. No expsrimental data are given. The study is non-GLP and non-guideline.

26-SEP-2005 (66)

5.6 Genetic Toxicity 'in Vivo'

5.7 Carcinogenicity

Species: rat Sex: male
Strain: Sprague-Dawley
Route of administration: oral feed
Exposure period: up to 27 or 44 weeks
Frequency of treatment: daily (feeding study)
Doses: 0.84 % in diet
Result: negative
Control Group: yes

Method: other: no standardized method used
Year: 1975
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Male rats were fed diets containing Na2SO4. The study was part of a toxicity study on Azo Dyes. The sodium sulfate were included as control series.
METHOD OF CALCULATION:
not described

Result: MORTALITY: no mortality was observed (10 surviving rats in both series) in both test series after 27 and 44 weeks of exposure as compared to control (10 surviving rats).
CLINICAL SIGNS: No tumors were detected. No evidence of hyperplastic and/or dysplatic change after 16 weeks. No cholangiofibrosis or mild cirrhosis in the liver after 16 weeks were observed as compared to control.

BODY WEIGHT CHANGES: No significant differences in overall body weight gain or in liver weight were observed.

_group	Eff.no. of rats	starting weight g +/- SD mean	no. of rats surviving	Terminal body wght g +/- SD mean	Terminal liver wght g +/- SD mean
Control					
a	5	230.8-18.6	2	358.5	10.11
b	5	193.4 33.6	5	358.4-16.0	10.2-0.49
Na2SO4					
a	5	252.0-30.2	3	414.7-39.5	14.3-1.42
b	5	194.2-35.7	5	332.0-53.7	10.03-0.99

FOOD AND WATER CONSUMPTION CHANGES: no changes observed

Test condition: TEST ORGANISMS
- Age: not described
- Weight at study initiation: mean weight of animals 211.6 gram
- Number of animals: total 90 , 5 in a cage
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: Study was divided in two series. One series lasted 27 weeks, and the other 44 weeks
- Type of exposure: feeding study, daily feeding

- Post exposure period: no
FOR ORAL STUDIES:
- Vehicle: maize oil
- Concentration in vehicle: 8.4 gram/kg
- Total volume applied: 30 ml
- Doses: 0.84 % in diet
CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: yes
- Food consumption: Basal diet consited of pellets with 15-16% protein, 6-8% fat and 8-9 % fibre (Victoria Wheat growers Corp. Ltd, Melbourne, Aus.). The consumption rate was 10 g/rat per day at the start up to 17 g/rat per day at the end of the study.
- Water consumption: free acces to tap water
- Clinical signs: not described
- Mortality: yes
- Macroscopic examination: yes
- Ophthalmoscopic examination: not described
- Haematology: yes, haemoglobin estimations were performed.
- Clinical chemistry: not described
- Urinalysis: not described
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: spleen, liver
- Microscopic: not described
OTHER EXAMINATIONS: lung sections were examined after staining with haematoxylin, eosin and the PAS method.
STATISTICAL METHODS: The probability of observing liver tumors of 1 cm or more in diameter, and evidence of metastatic spread or multiple tumors at death was calculated by an actuarial method, as described by Pilgrim and Dowd, Cancer Res. 23, 45 (1963). Differences between numbers rats bearing tumours of at least 1 cm diameter, were compared using Fisher's exact test.

Reliability: (3) invalid
No guideline study, 5 male animals only

26-SEP-2005 (16)

Species:	mouse	Sex: male/female
Strain:	Swiss	
Route of administration:	s.c.	
Exposure period:	26 weeks	
Frequency of treatment:	weekly	
Doses:	31 µg in 0.01 ml sodium chloride (0.9%) per g body weight / week	
Result:	negative	
Control Group:	other: Na2SO4 served as control for 4-HMBD / historical controls	
Method:	other: see freetext	
Year:	1987	
GLP:	no	
Test substance:	as prescribed by 1.1 - 1.4	

Method: METHOD FOLLOWED: Test was control test of investigation of carcinogenity of 4-(hydroxymethyl)benzenediazonium ion in mice. Mice were treated for 26 weeks, and observed for 150 weeks, to test substance and control (Na2SO4)
METHOD OF CALCULATION:
not described

Result: MORTALITY AND TIME TO DEATH: see attachement, table I

CLINICAL SIGNS: see attachment, table II
BODY WEIGHT GAIN: not described
FOOD/WATER CONSUMPTION: not described
GROSS PATHOLOGY: see attachment, table II
HISTOPATHOLOGY: see attachementm, table II
OTHER: see attachment, table II
TIME TO TUMOURS: see attachment, table II
STATISTICAL RESULTS: not described

Test condition: TEST ORGANISMS
- Age: 6 weeks (50:50 male/female)
- Weight at study initiation: not described
- Number of animals: 50 male and 50 female
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 26 weeks
- Type of exposure: subcutaneously injections weekly
- Post exposure period: not described
FOR ORAL STUDIES:
- Vehicle: 0.9 %v sodium chloride
- Concentration in vehicle: 31 µg per 0.01 ml vehicle per g body weight
- Total volume applied: not described
- Doses: weekly
CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: yes
- Food consumption: no
- Water consumption: no
- Clinical signs: yes
- Mortality: yes
- Macroscopic examination: yes
- Ophthalmoscopic examination: no
- Haematology: no
- Clinical chemistry: no
- Urinalysis: no
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic Histological study: skin, subcutis, liver, spleen, kidneys, bladder, thyroid, heart, pancreas, testes, ovaries, uterus, nasal turbinals, lungs
- Microscopic: Yes, after staining with hematoxylin and eosin
OTHER EXAMINATIONS: All other pathological changes
STATISTICAL METHODS: not described

Attached doc.: RS2-Toth.doc
Reliability: (3) invalid
26-SEP-2005 (97)

5.8.1 Toxicity to Fertility

Type:	other: two parities using the same mice
Species:	mouse
Sex:	female
Strain:	ICR
Route of administration:	drinking water
Exposure Period:	1 week prior to breeding until study termination
Frequency of treatment:	drinking water was avaialble ad libitum
Premating Exposure Period	
male:	no exposure
female:	1 week
Duration of test:	1 week prior to breeding until study termination
No. of generation studies:	1
Doses:	0, 0.924, 1.848, 3.696, 7.392 g/liter

Control Group: other: One control group received deionized distilled water and one received deionized distilled water with 2,392 ppm Na
NOAEL Parental: >= 7392 mg/l
NOAEL F1 Offspring: >= 7392 mg/l
other: NOAEL F1 Offspring 2 :
>= 7392 mg/l
Result: No effects on litter size and weaning weight were seen. Reproductive performance is not affected in this study.

Method: other: not specified
Year: 1988
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS: ICR mouse
ADMINISTRATION / EXPOSURE
- Type of exposure: drinking water
- Duration of test/exposure: 1 week before study until study termination.
- Treatment: drinking water was available ad libitum
- Control group and treatment: One control group received deionized distilled water and one received deionized distilled water with 2,392 ppm Na
- Vehicle: deionized water
- Concentration in vehicle: 0, 0.924, 1.848, 3.696, 7.392 g/liter
- Total volume applied: -
- Doses: drinking water with 0, 0.924, 1.848, 3.696, 7.392 g/liter sodium sulfate ad libitum.
- Concentrations: -
- Particle size: -
- Type or preparation of particles:-
MATING PROCEDURES:
After one week a male mouse that had received tap water only was randomely bred withe ach female mouse. The female was checked every day for a vaginal plug. When a vaginal plug was observed the male was removed.
STANDARDIZATION OF LITTERS:
The litter were standardized to 8 pups per litter. The dams with fewer tahn 8 pups received pups from other dams in the same dose group. If these were not available they were assigned pups from a lower dose group.
PARAMETERS ASSESSED DURING STUDY P AND F1(1) AND F1(2):
- Clinical observations:
water consumption was measured daily during the 2nd and 3rd week of gestationa and 1st and 2nd week of lacation. (the measureemnts during week 1 of gestation were discarted due to leakage from drinking bottles, the measurements performed during week 3 of lacation were also discarted because the pups started drinking water).
Bodyweights of the dams were recorded at parturition and litter sizes were determined.
At 21 days pp the dams and litters were weighed.
- Estrous cycle: -
- Sperm examination: -
- Others: -
OFFSPRING: -
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Organ weights P and F1: -

- Histopathology P and F1: -
- Histopathology F1 not selected for mating, F2: -
OTHER EXAMINATIONS: -
STATISTICAL METHODS:
The description of the statistical analysis remains unclear: The least square mean analysis of variance technique was used to analyze the data. One contrast was used to compare the different groups. Sulfate treatment effects were partitioned into linear, quadratic and cubic components using orthogonal contrasts. Student's t-test were used to determine the difference in water consumption between weeks in both gestation and lactation.

Result:
NOAEL (NOEL): 7392 mg/l = 5000 ppm
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX:
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Parental data and F1:
- Body weight: gestational and lactational body weight gian was not influenced by level of sulfate consumed.
- Food/water consumption: a decrease in water consumption was seen. It is suggested that the amials became acclimated to the high sulfate levels because the water consumtion levels ere higher during the 2nd week of lactation comared to the 1st week during the 2nd parity.
- Description, severity, time of onset and duration of clinical signs: -
- Fertility index: -
- Precoital interval: -
- Duration of gestation: -
- Gestation index: -
- Changes in lactation: -
- Changes in estrus cycles: -
- Effects on sperm: -
- Hematological findings incidence and severity:-
- Clinical biochemistry findings incidence and severity: -
- Mortality: 0
- Gross pathology incidence and severity: -
- Number of implantations: -
- Number of corpora lutea: -
- Ovarian primordial follicle counts: -
- Organ weight changes: -
- Histopathology incidence and severity: -
- Offspring toxicity F1 and F2: -
- Litter size and weights: litter size was not affected by treatment.
- Sex and sex ratios: -
- Viability index: none of the pups died.
- Post natal survival until weaning: none of the pups died.
- Effects on offspring: -
- Postnatal growth, growth rate: -
- Vaginal opening (F) or preputial separation (M): -
- Other observations; -
STATISTICAL RESULTS: -

Test substance:
Sodium sulfate, reagent grade.

Reliability:
(4) not assignable
Non-GLP and non-guideline study. Not sufficiently detailed. The set up of the study differs from the standard. Mice were exposed from 1 week before the study until study termination. The same female mice gave birth to the first and the second litter. The litter was weaned at 21 days pp and the mice were mated again.The males were not exposed. Possibly only the mice with two subsequent litters were

involved in the analysis.

27-SEP-2005 (7)

5.8.2 Developmental Toxicity/Teratogenicity

Species:	mouse	Sex: female
Strain:	other: ICR/SIM	
Route of administration:	other: oral (gavage)	
Exposure period:	4 days (gestation day 8-12)	
Frequency of treatment:	once daily	
Duration of test:	up to day 22 of pregnancy	
Doses:	2800 mg/kg/day	
Control Group:	other: yes (N=28, vehicle alone H2O)	

Method: other: no guideline study
Year: 1986
GLP: no

Result: As part of a validation of a developmental screen, pregnant mice were exposed to 55 compounds, composed of known teratogens, known non-teratogens or equivocal substances.
Exposure: single daily dose by gavage; dose level at or near induction of maternal toxicity.
Vehicle alone (H20): 15 control groups of 28-30 mice.
Vehicle alone (Corn oil): 13 control groups of 28-30 mice.

Endpoints: maternal weight gain, delivery rate, litter size, % live birhts, pup weight day 1 and day 3, neonatal survival rate, macrospoci visceral and skeletal abnormalities
Statistical analysis:
maternal weight :two-tailed analysis of variance
live and dead litter size: one-tailed analysis of variance
neonatal survival rate: Fisher one-tailed exact probability.
neonatal weight: two-tailed analysis of variance with litter size as co-variant
Overal results: reported "Seidenberg JM , Becker RA: A summary of the results of 55 chemiclas screened for developmental toxicity im mice. Teratogenesis, Carcinogenesis, Mutagenesis 7:17-28 (1987)
Results for sodium sulfate:
Compared to controls, slight increase in neonatal body weigh at day 1 pp.(1.80+0.14 vs 1.72 + 0.13 grams).
Normal maternal weight gain, normal delivery rate, normal litter size, normal nr. of live births, normal weight of pups on day 3, no macroscopic visceral or sceletal abnormalities
Test substance: Na2SO4, not specified
Reliability: (2) valid with restrictions
non-standard screening test.

26-SEP-2005 (90)

Species:	mouse	Sex: female
Strain:	other: ICS/SIM	
Route of administration:	other: oral (gavage)	
Exposure period:	4 days (gestation day 8-12)	
Frequency of treatment:	once daily	
Duration of test:	up to day 22 of pregnancy	
Doses:	Na2SO4: 2800 mg/kg	
Control Group:	other: yes (N=28, vehicle alone H2O)	

Method: other: no guideline study

Year: 1987
GLP: no

Remark: Reviewer disagrees, slight increase in body weight of neonates on day 1 p.p. only is not an adverse effect and is biologically totally irrelevant.

Result: Summary of results of a screening study fully described in:
Seidenberg JM, Anderson DG, ecker RA: validation of an in vivo developmental screen in the mouse. Teratogenesis, Carcinogenesis and Mutagenesis, 6:361-374 (1986) See RS
Overal results:
24 of 26 substances previously reported as positive in teratogenicity / embryotoxicity tests scored positive in this screen.
93% of substances previously reported as negative scored negative in this screen.
equivocal substances 4of 5 positive in this screen
no data: 3 out of 9 considered positive, among them sodium sulfate.
Results for sodium sulfate:
Compared to controls, slight increase in neonatal body weigh at day 1 pp.(1.80+ -0.14 vs 1.72 + -0.13 grams).
Normal maternal weight gain, normal delivery rate, normal litter size, normal nr. of live births, normal weight of pups on day 3, no macroscopic visceral or sceletal abnormalities; Considered by authors as a positive outcome of screening
test.

Test substance: Na2SO4, not specified

Reliability: (2) valid with restrictions
non-standard screening test.; scoring criteria too strict.

27-SEP-2005 (89)

Species: mouse Sex: female
Strain: other: CF-1
Route of administration: s.c.
Frequency of treatment: single injection at day 8 or 9 of gestation
Duration of test: not described
Doses: 60 mg/kg bw
Control Group: yes
Result: increased maternal weight gain, no soft tissue abnormalities, increase of skeletal abnormalities (delayed ossification)

Method: other: no standardized method used
Year: 1973
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: The teratogenic effects of sodium sulfate injected s.c. in albino mice was investigated. The study examined mice after administration at day 8 and 9 of gestation.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described

Result: NOAEL (NOEL), LOAEL (LOEL): not determined
MATERNAL TOXIC EFFECTS BY DOSE LEVEL:
- Mortality and day of death: not described
- Number aborting: not described
- Number of resorptions: See attachement
- Duration of Pregnancy: not described

- Body weight: see attachement
- Food/water consumption: not described
- Description, severity, time of onset and duration of clinical signs: Soft tissue abnormalities were not significantly different from the control group. Skeletal abnormalities , described as delayed ossification, especially in phalanges, sternebrae and skull, were statistically different form control group .
- Hematological findings incidence and severity: not described

- Clinical biochemistry findings incidence and severity: not described
- Gross pathology incidence and severity:
- Organ weight changes:
- Histopathology incidence and severity:

FETAL DATA:
- Litter size and weights: 6, no weight determined
- Number viable: 51 fetuses
-·Sex ratio: not determined
- Postnatal growth: not described
- Postnatal survival: not described
- Grossly visible abnormalities: no abnormalities
- External abnormalities: see attachement, no abnormalities
- Soft tissue abnormalities: see attachement, no abnormalities
- Skeletal abnormalities: see attachement, no abnormalities

STATISTICAL RESULTS: not described

Test condition: TEST ORGANISMS:
Albino mice (CF-1) (25-30 gram), obtained from Carworth Farms, Inc. New York, USA.
ADMINISTRATION / EXPOSURE
- Type of exposure: injection subcutaneous
- Duration of test/exposure: as described by Iuliucci, J.D., Gautieri, R.F., J. Pharm. Sci, 60:420 (1971).
- Treatment: at day 8 or 9 of gestation
- Control group and treatment: yes, untreated (saline)
- Vehicle: distilled water
- Concentration in vehicle: 10 mg/ml
- Total volume applied: not described
- Doses: one injection
- Concentrations: 60 mg/kg body weight

PARAMETERS ASSESSED DURING STUDY:
- Body weight gain: yes, ratio between start and end of study
- Food consumption: no
- Clinical observations: yes, soft tissue abnormalities, skeletal abnormalities and resorption uterine horns
- Examination of uterine content: no
- Examination of fetuses: yes
- Litter : yes

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
OTHER EXAMINATIONS: Exencephaly, Axial skeletal fusions and cryptorchid testes.
STATISTICAL METHODS: as described by Iuliucci, J.D., Gautieri, R.F., J. Pharm. Sci, 60:420 (1971).

Attached doc.: RS1-Arcuri&Gautieri.doc

Reliability: (2) valid with restrictions
Not a guideline study. Experiment described in detail. Not

all parameters determined. Endpoints are not all clearly described.

27-SEP-2005 (9)

5.8.3 Toxicity to Reproduction, Other Studies

5.9 Specific Investigations

5.10 Exposure Experience

Type of experience: Human - Epidemiology

Method: Method: Cross-sectional study, internal sub-cohort study
Subjects: 119 male workers from natural sodium sulfate mines.
Age range: 17 to 58
exposure duration: 0.6-31 years
(no control group, study outcomes compared with "normal values", source not given).
Exposure: Na2SO4 dust ,range 5 mg/m3 to 150 mg/m3
(sampling method, strategy, number, frequency and timespan of sampling not given).

Result: General medical screening, lung function tests, blood pressure, skin condition, gastro-intestinal functioning, serum sodium, calcium, potassium chloride and sulfate content were all within normal ranges (i.e presumably as found in the general population).

Mean urinary excretion of inorganic sulfate exceeded 2.2 gr/liter in all workers and thirty percent of the workers excreted more than 3 gr of inorganic sulfate per day, indicating massive uptake from recent exposure. The only subjective symptom indicated by the workers was nasal irritation and runny noses on exposure to dust.

Internal sub-cohort study:
Short exposure duration subcohort:
subjects: More than 10 years of exposure (n=77)
age 28.0 +-10,
exposure duration 3.1 + 2.8 years
Long exposure duration subcohort:
Subjects: more than 10 years exposure (n=42)
age 454.5 + 8.8,
exposure duration 19.9 + 3.6 years
Results:
No differences other than explained by age difference.

Reliability: (2) valid with restrictions
Absence of control group, incomplete description of exposure
and possibility for healthy worker effect severely restrict extrapolation

01-DEC-2004 (59)

Type of experience: Livestock - Exposure through Feeding

Remark: Method:
31 sows and 27 gilts were each allotted to three treatments to study the effect of water quality during gestation and lactation. Sulfate was added to the water at concentrations

in three treatments (1) 320 - 620 mg/l (2) 1820 - 2840 mg/l (3) 3320 - 5080 mg/l. Water was offered ad libitum. from 30 days post-breeding through 28 days lactation.
Results:
There was no significant difference in gestation or lactation, number or weight of pigs at birth or at weaning. Water consumption did not differ during gestation, but increased as salt levels increased. Water consumption was 13.6, 14.2 and 16.8 liter/day for lactating females in treatment 1, 2 and 3.
These results suggests that sulfates up to and including 3320 mg/l, in water have no significant effect on reproduction in the gilt or sow.

Reliability: (3) invalid

Documentation insufficient for assessment

07-NOV-2001 (79)

Type of experience: other: Human - controlled study

Remark: METHOD:
The objective of the study was to provide additional information regarding whether sensitive populations (infants
and transients) may be adversely affected by sudden exposure
to drinking water containing high levels of sulfate.

One hundred and five study participants were divided among the dose groups as follows: 24
received 0 mg/L sulfate; 10 received 250 mg/L sulfate; 10 received 500 mg/L sulfate; 33 received 800
mg/L sulfate; and 28 received 1200 mg/L sulfate. The number of bowel movements recorded each day by study participants were analyzed. There were no statistically significant differences in the bowel movements among the groups on days 3, 4, 5, or 6. There were also no statistically significant differences in the bowel movements reported when comparing days 1 and 2 (the days when there was no sulfate in the water) with days 3, 4, and 5 within each dose group. To examine the data for a trend toward increased frequency of reports of diarrhea with increased dose of sulfate, a logistic regression model were the dose as an ordinal variable was included for osmotic diarrhea was included. There was no statistically significant increase in reports of diarrhea with increasing dose (one-sided p = 0.099).

RESULTS:

One hundred five study participants were divided among the dose groups as follows: 24 received 0 mg/L sulfate; 10 received 250 mg/L sulfate; 10 received 500 mg/L sulfate; 33 received 800 mg/L sulfate; and 28 received 1200 mg/L sulfate. The demographic information for the study population was as follows: the mean age of participants was 42 years; the majority (62%) was female;
the races included in the study population were white (80%), black (13%), and Asian/Pacific Islander (7%). Ninety-five percent of the participants were non-Hispanic.

In the experimental trials with adult volunteers, no significant dose-response association between acute exposure to sodium sulfate in water (up to 1200 mg/L) and reports of diarrhea were found.
However, a weak (not statistically significant) increase in reports of diarrhea at the highest dose level when it was compared to the combined lower doses was observed.

Remark: concentration in drinking water known, but not actual dose.

Reliability: (4) not assignable
Documentation insufficient for assessment: Abstract only.

27-SEP-2005 (76)

Type of experience: Human

Remark: Inhalation of sodium sulfate dust causes irritation of the mucuous membranes, and prolonged skin contact has a drying effect.

Reliability: (3) invalid
Documentation insufficient for assessment.

27-SEP-2005 (101)

Type of experience: Livestock - Exposure through Feeding

Remark: Association between sulfate in drinking water and diarrhea in swine was investigated. Sulfate concentrations ranged from 5.99 to 1629 mg/l recorded at 54 farms in Ohio USA. Associations between sulfate concentrations and prevalence of diarrhea could not be established.

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (107)

Type of experience: Human - Epidemiology

Remark: Evaluation of infant diarrhea associated with elevated levels of sulfate in drinking water.

Method:
274 households were investigated in South-Dakota USA.
Sulfate concentrations in drinking water was determined.
Data on infant diarrhea were collected using questionnaires.
Logistic regression was used to estimate the risk for diarrhea.

Results:
69% of the households drank municipal water and 54% used it in the infants diet. 39 infants developed diarrhea. Of the 170 households that submitted water samples, 141 were using the water in the infants diet. The median sulfate concentration of the water was 264 mg/l. 25 infants developed diarrhea.
Average infant daily sulfate intake was not significantly associated with an increase diarrhea rate. There was no significant association between sulfate intake and the incidence of diarrhea for the range of sulfate studies. There was no effect of a dose-response or threshold effect.

Reliability: (4) not assignable

Only secondary literature available

09-NOV-2001 (39)

Type of experience: Livestock - Exposure through Feeding

Remark: Artificially reared neonatal piglets were used to study the effect of inorganic sodium sulfate on bowel function in human infants.

Method:
Two experiments were conducted to evaluate the effect of high levels of inorganic sulfate intake on the growth, feed intake and feaces consistency.
40 pigs with an average age of 5d were individually caged abd reared with an automatic feeding device. Ten pigs per dietary treatment were fed one of four diets containing the following levels of inorganic sodium sulfate (mg/l diet): 0, 1200, 1600, 2000 for exp 1 (18 days study), and 0, 800, 2000, 22000 for exp. 2 (16 days study).

Results:
The levels of sulfate did not affect (P>0.05) the growth of piglets, or their food intake. 1200 mg/l sulfate had no effect on feaces consistency, while 1800 mg/l sulfate did (non-pathogenic diarrhea). Added sulfate did not affect (P> 0.05) relative kidney weight. The results suggest that the level of added dietary inorganic sulfate at which 50% of piglets develop nonpathogenic diarrhea is between 1600 and 1800 mg/l.

Reliability: (2) valid with restrictions
Acceptable, well documented study.

22-JUN-2005 (43)

Type of experience: Direct observation, poisoning incidents

Remark: Two outbreaks of poisoning (eosinophilic meningoencephalitis) in pigs due to treatment with sodium sulfate. Experimental reproduction indicated a similar syndrome.

Method:
8 12 weeks old pigs were each given by drneching gun 50 gram of sodium sulfate, dissolved in a minimum amount of water daily for 3 consecutive days. Controls were treated with water.
Results:
2 of the treated pigs were found dead on day 4, and 3 were in prostrate and in extremis. The latter 3 animals were killed for examination. The three were all inco-ordination, blind and had epileptiform convulsions. Histopathological examination revelaed lesions of the central nervous system, vacuolation, nueronal degeneration, cortical laminar malacia. Large numbers of eosinophils and some macrophages were present in the meninges and in the perivascular spaces in the cortical white matter.

Reliability: (3) invalid

Documentation insufficient for assessment

22-JUN-2005 (32)

Type of experience: Human - Exposure through Food

Remark: Three illustrative cases of diarrhea in infants in Canada following ingestion of well waters with a sulfate content above 600 mg/l. Other causes such as infections or other presence of chemicals were excluded. The estimated daily dose would have been around 70- 100 mg/kg/day.
It is recommended that water with more than 400 mg/l sulphate be regarded as unsuitable for infant feeding.

Remark: clinically, cause and effect relationship clearly established. Extrapolation to general population not possible in the absence of data on the population at risk and incidence

Reliability: (4) not assignable
27-SEP-2005 (25)

5.11 Additional Remarks

Type: Toxicokinetics

Remark: Review:

Sulfate is a normal constituent of the blood and is a normal metabolite of sulfur-containing amino acids, and excess sulfate is excreted in the urine. Daily sulfate excretion is reported to be 0.20 to 0.25 mmol/kg bw/day and higher in children.

In male adult Wistar rats, approximately 73% of dietary calcium or magnesium sulfate salts was absorbed, although absorption was partly dependent on other dietary elements.

Reliability: (4) not assignable

29-SEP-2005 (50)

Type: other: Oral toxicity to pigs

Remark: Sodium sulfate (Glauber's salt) toxicity was observed in pigs after drenching eight-week old pigs with 50 g sodium sulfate for three days, and restricting their water supply. The animals showed nervous signs, twitching, tremors and convulsions. The most noticeable lesion at post mortem was widespread vacuolation and necrosis of the cerebral cortex. The sodium concentration of the cerebrospinal fluid was significantly higher than normal.

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (26)

(1) Adams, A.W., Cunningham, F.E., Munger, L.L. (1975). Some effects on layers of sodium sulfate and magnesium sulfate in their drinking water. Poultry Sci. 54(3):707-714.

(2) Allgemeine Verwaltungsvorschrift (1990). Uber die nahere bestimmung wassergefahrdender stoffe und ihre einstufung entsprechend ihrer gefahrlichkeit-VwV wassergefahrende stoffe (VwVwS) 9.3.1990.

(3) Ambient water Quality Guidelines for sulphate (2000). Ministry of Environment, Lands and Parks Province of British Columbia, Water Quality Section Water Management Branch Victoria, BC, Canada.

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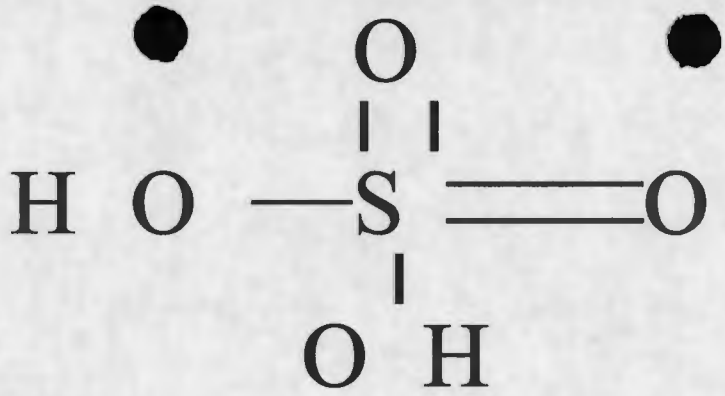
Appendix XI: ECOSAR Modeling Results



ECOSAR Version 1.11 Results Page

SMILES : OS(=O)(=O)O
User SMILES: [O-]S(=O)(=O)O.[Na+]
CHEM : SULFURIC ACID, MONOSODIUM SALT
CAS Num: 007681-38-1
ChemID1:
MOL FOR: H2 O4 S1
MOL WT : 98.07
Log Kow: -2.200 (EPISuite Kowwin v1.68 Estimate)
Log Kow: (User Entered)
Log Kow: (PhysProp DB exp value - for comparison only)
Melt Pt: (User Entered for Wat Sol estimate)
Melt Pt: 10.31 (deg C, PhysProp DB exp value for Wat Sol est)
Wat Sol: 1E+006 (mg/L, EPISuite WSKowwin v1.43 Estimate)
Wat Sol: (User Entered)
Wat Sol: 1E+006 (mg/L, PhysProp DB exp value)

Values used to Generate ECOSAR Profile

Log Kow: -2.200 (EPISuite Kowwin v1.68 Estimate)
Wat Sol: 1E+006 (mg/L, PhysProp DB exp value)

Available Measured Data from ECOSAR Training Set

No Data Available

ECOSAR v1.11 Class-specific Estimations

Inorganic Compound

```
*************************************************************************
* NOTE: METAL ([Na], [Li] or [K]) HAS BEEN REMOVED FOR PROPER ESTIMATION. *
* SALTS SHOULD BE ENTERED IN ECOSAR AS THE NEUTRAL NON-SALT FORM OF THE   *
* MOLECULE CORRESPONDING TO EITHER THE FREE BASE OR CONJUGATE ACID.       *
* SEE HELP MENU FOR MORE INFORMATION                                      *
*************************************************************************
```

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Neutral Organic SAR	: Fish	96-hr	LC50	4.77e+005
(Baseline Toxicity)	: Daphnid	48-hr	LC50	1.84e+005
	: Green Algae	96-hr	EC50	27531.549
	: Fish		ChV	29497.303
	: Daphnid		ChV	6088.096
	: Green Algae		ChV	3039.855

Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect. If the effect level exceeds the water solubility by 10X, typically no effects at saturation (NES) are reported.

Class Specific LogKow Cut-Offs

If the log Kow of the chemical is greater than the endpoint specific cut-offs presented below, then no effects at saturation are expected for those endpoints.

Inorganic Compound:

Maximum LogKow: 5.0 (LC50)
Maximum LogKow: 6.4 (EC50)
Maximum LogKow: 8.0 (ChV)

Baseline Toxicity SAR Limitations:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)

Appendix XII. Notification of Filing (NOF)

EPA REGISTRATION DIVISION COMPANY NOTICE OF FILING FOR PESTICIDE PETITIONS PUBLISHED IN THE FEDERAL REGISTER

EPA Registration Division contact: PV Shah, 703-308-1846

INSTRUCTIONS: **Please utilize this outline in preparing the pesticide petition. In cases where the outline element does not apply, please insert "NA-Remove" and maintain the outline. Please do not change the margins, font, or format in your pesticide petition. Simply replace the instructions that appear in green, i.e., "[insert company name]," with the information specific to your action.**

TEMPLATE:

Ecolab, Inc.

[Insert petition number]

EPA has received a pesticide petition **([insert petition number])** from Ecolab, Inc., EPA Company Number 1677, 370 N. Wabasha Street, St. Paul, MN 55102 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180.

(Options (pick one)

2. to establish an exemption from the requirement of a tolerance for

Sodium Bisulfate, CAS No. 7681-38-1, for use as an inert ingredient in antimicrobial pesticide formulations applied to food-contact surfaces in public eating places, dairy processing equipment and food processing equipment and utensils in accordance with 40 CFR §180.940(a). EPA has determined that the petition contains data or information regarding the elements set forth in section 408 (d)(2) of FDDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism.* Not applicable to this inert ingredient petition

2. *Analytical method.* Not applicable to this inert ingredient petition

3. *Magnitude of residues.* Not applicable to this inert ingredient petition

B. Toxicological Profile

1. *Acute toxicity.* Because bisulfate/sulfate anion is a naturally-occurring constituent in many food substances and a mammalian (human) metabolite, the existing toxicology database is limited. Since the bisulfate anion is converted to sulfate in solution, toxicology studies for sodium sulfate are generally considered as relevant for sodium bisulfate as well.

The World Health Organization (WHO, 2010a) reported a low level of acute oral toxicity in mammals, including 2800 mg/kg bw in male rats and >2500 mg/kg bw in female rats. The oral LD_{50} results from the rat toxicity study are equivalent to EPA Toxicity Category III.

Sodium bisulfate is not irritating to skin.

2. *Genotoxicty.* There are no reported genotoxicity studies for sodium bisulfate and it is not listed as a carcinogen by NTP, IARC, or OSHA.

The UNEP (2005) SIDs for Sodium Sulfate reported negative AMES results. Additionally, UNEP reported that a non-GLP chronic feeding study (1975) in which male Sprague-Dawley rats were fed 0.84% sodium sulfate in the diet for up to 27 and 44 weeks as the control in a toxicity study for Azo Dyes did not result in mortality or the formation of tumors. Moreover, there were no significant differences in overall body weight gain or in liver weight.

3. *Reproductive and developmental toxicity.* Groups of pregnant CF-1 albino mice were injected subcutaneously on gestation day 8 or 9 with sodium sulfate at 60 mg/kg bw given as 10 mg/ml in water. Although skeletal abnormalities were observed in both groups, the difference seen from saline controls after dosing on day 9 of gestation was not significant, and the anomalies did not appear to involve fusions of the axial skeleton.

Pregnant ICR/SIM mice were given a saturated aqueous solution of sodium sulfate orally by gavage, with a dose of 2800 mg/kg bw/day on days 8-12 of gestation. No maternal deaths occurred and the average maternal weight gain during the treatment period was not significantly different from that of water-treated controls. Twenty-four litters were delivered alive, and none were resorbed. The mean numbers of neonates delivered alive and dead in each litter and the survival of neonates on day 3 were not statistically significantly different from those of controls.

4. *Subchronic toxicity.* Due to its naturally occurring prevalence in food, subchronic toxicity data specific to sodium bisulfate are not readily available.

5. *Chronic toxicity.* Due to its naturally occurring prevalence in food, chronic toxicity data specific to sodium bisulfate are not readily available.

6. *Animal metabolism.* Sodium bisulfate mammalian metabolism is essentially that of sodium cation and sulfate anion. When sodium hydrogen sulfate is added to food products containing water or after ingestion of sodium hydrogen sulfate, it ionizes to sodium ions, hydrogen ions and sulfate ions.

Excess sulfate anions, naturally-occurring components in food and a metabolite of *in vivo* sulfur oxidation, are highly water soluble and therefore eliminated in urine unchanged without the formation of toxic metabolites.

7. *Metabolite toxicology.* There are no metabolites of toxicological concern.

8. *Endocrine disruption.* EPA did not report having any available information to suggest that sodium bisulfate would have any endocrine effects. When the appropriate screening and/or testing protocols under the EDSP have been developed, sodium bisulfate may be subject to additional screening and/or testing to better characterize effects related to endocrine disruption. This does not impact the current regulatory status of sodium bisulfate.

C. Aggregate Exposure

1. *Dietary exposure.* In the Reregistration Eligibility Decision Document for Mineral Acids (1993), EPA stated: "The four mineral acids [which included sodium bisulfate] pose no human dietary risks. People may be exposed to these chemicals when they are used as antimicrobials, however this exposure involves such dilute solutions that it is believed to be inconsequential."

i. *Food.* Sodium bisulfate (and its hydrolyzed congener sodium sulfate) occurs naturally (at non-toxic levels) in many food products, which humans may be exposed to on a daily basis without apparent harmful effects.

ii. *Drinking water.* Sulfates can occur naturally in drinking water. A 1999 United States Environmental Protection Agency and Centers for Disease Control and Prevention on the health effects from exposure to high levels of sulfate in the drinking-water in two sensitive populations (infants and transient adults) did not show statistically significant effects.

2. *Non-dietary exposure.* Residential exposure could come from use of sodium bisulfate in consumer products, such as a toilet bowl cleaners. There are no risk concerns for these exposures.

D. Cumulative Effects JECFA (2010) confirms that bisulfate/sulfate anions do not constitute toxic metabolites. Thus, the Agency would assume that sodium bisulfate does not have a common mechanism of toxicity with other substances. As a result, any potential human health risks would be those that result only from the use of sodium bisulfate as a household use sanitizer for toilet bowls and as an inert ingredient in pesticide formulations applied to growing crops according to 40 CFR §180.920 applications.

E. Safety Determination

1. *U.S. population.* EPA has not reported toxicological endpoints of concern for the current non-food residential use and the use as an inert ingredient in pesticide formulations according to 40 CFR §180.920 applications. Based on this, EPA has determined that a quantitative risk assessment is not required for sodium bisulfate. The anticipated food, drinking water and residential exposure should not be of concern since toxicological endpoints for risk assessment were not identified based on the available data.

2. *Infants and children.* The safety determination for infants and children considers factors of the toxicity, use practices, and environmental behavior noted above for the general population, but also takes into account the possibility of increased dietary exposure due to the specific consumption patterns of infants and children, as well as the possibility of increased susceptibility to the toxic effects of sodium bisulfate residues in this population subgroup. The Agency has previously determined that there are no additional risks to infants and children from sodium bisulfate. The inclusion of the uses supported by adding the tolerance exemption at 40 CFR § 180.940(a) would not change this determination.

F. International Tolerances

Currently, there are no CODEX MRLs established for sodium bisulfate.

EPA REGISTRATION DIVISION COMPANY NOTICE OF FILING FOR PESTICIDE PETITIONS PUBLISHED IN THE FEDERAL REGISTER

EPA Registration Division contact: PV Shah, 703-308-1846

INSTRUCTIONS: **Please utilize this outline in preparing the pesticide petition. In cases where the outline element does not apply, please insert "NA-Remove" and maintain the outline. Please do not change the margins, font, or format in your pesticide petition. Simply replace the instructions that appear in green, i.e., "[insert company name]," with the information specific to your action.**

TEMPLATE:

Ecolab, Inc.

[Insert petition number]

EPA has received a pesticide petition **([insert petition number])** from Ecolab, Inc., EPA Company Number 1677, 370 N. Wabasha Street, St. Paul, MN 55102 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180.

(Options (pick one)

2. to establish an exemption from the requirement of a tolerance for

Sodium Bisulfate, CAS No. 7681-38-1, for use as an inert ingredient in antimicrobial pesticide formulations applied to food-contact surfaces in public eating places, dairy processing equipment and food processing equipment and utensils in accordance with 40 CFR §180.940(a). EPA has determined that the petition contains data or information regarding the elements set forth in section 408 (d)(2) of FDDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism.* Not applicable to this inert ingredient petition

2. *Analytical method.* Not applicable to this inert ingredient petition

3. *Magnitude of residues.* Not applicable to this inert ingredient petition

B. Toxicological Profile

1. *Acute toxicity.* Because bisulfate/sulfate anion is a naturally-occurring constituent in many food substances and a mammalian (human) metabolite, the existing toxicology database is limited. Since the bisulfate anion is converted to sulfate in solution, toxicology studies for sodium sulfate are generally considered as relevant for sodium bisulfate as well.

The World Health Organization (WHO, 2010a) reported a low level of acute oral toxicity in mammals, including 2800 mg/kg bw in male rats and >2500 mg/kg bw in female rats. The oral LD_{50} results from the rat toxicity study are equivalent to EPA Toxicity Category III.

Sodium bisulfate is not irritating to skin.

2. *Genotoxicity.* There are no reported genotoxicity studies for sodium bisulfate and it is not listed as a carcinogen by NTP, IARC, or OSHA.

The UNEP (2005) SIDs for Sodium Sulfate reported negative AMES results. Additionally, UNEP reported that a non-GLP chronic feeding study (1975) in which male Sprague-Dawley rats were fed 0.84% sodium sulfate in the diet for up to 27 and 44 weeks as the control in a toxicity study for Azo Dyes did not result in mortality or the formation of tumors. Moreover, there were no significant differences in overall body weight gain or in liver weight.

3. *Reproductive and developmental toxicity.* Groups of pregnant CF-1 albino mice were injected subcutaneously on gestation day 8 or 9 with sodium sulfate at 60 mg/kg bw given as 10 mg/ml in water. Although skeletal abnormalities were observed in both groups, the difference seen from saline controls after dosing on day 9 of gestation was not significant, and the anomalies did not appear to involve fusions of the axial skeleton.

Pregnant ICR/SIM mice were given a saturated aqueous solution of sodium sulfate orally by gavage, with a dose of 2800 mg/kg bw/day on days 8-12 of gestation. No maternal deaths occurred and the average maternal weight gain during the treatment period was not significantly different from that of water-treated controls. Twenty-four litters were delivered alive, and none were resorbed. The mean numbers of neonates delivered alive and dead in each litter and the survival of neonates on day 3 were not statistically significantly different from those of controls.

4. *Subchronic toxicity.* Due to its naturally occurring prevalence in food, subchronic toxicity data specific to sodium bisulfate are not readily available.

5. *Chronic toxicity.* Due to its naturally occurring prevalence in food, chronic toxicity data specific to sodium bisulfate are not readily available.

6. *Animal metabolism.* Sodium bisulfate mammalian metabolism is essentially that of sodium cation and sulfate anion. When sodium hydrogen sulfate is added to food products containing water or after ingestion of sodium hydrogen sulfate, it ionizes to sodium ions, hydrogen ions and sulfate ions.

Excess sulfate anions, naturally-occurring components in food and a metabolite of *in vivo* sulfur oxidation, are highly water soluble and therefore eliminated in urine unchanged without the formation of toxic metabolites.

7. *Metabolite toxicology.* There are no metabolites of toxicological concern.

8. *Endocrine disruption.* EPA did not report having any available information to suggest that sodium bisulfate would have any endocrine effects. When the appropriate screening and/or testing protocols under the EDSP have been developed, sodium bisulfate may be subject to additional screening and/or testing to better characterize effects related to endocrine disruption. This does not impact the current regulatory status of sodium bisulfate.

C. Aggregate Exposure

1. *Dietary exposure.* In the Reregistration Eligibility Decision Document for Mineral Acids (1993), EPA stated: "The four mineral acids [which included sodium bisulfate] pose no human dietary risks. People may be exposed to these chemicals when they are used as antimicrobials, however this exposure involves such dilute solutions that it is believed to be inconsequential."

i. *Food.* Sodium bisulfate (and its hydrolyzed congener sodium sulfate) occurs naturally (at non-toxic levels) in many food products, which humans may be exposed to on a daily basis without apparent harmful effects.

ii. *Drinking water.* Sulfates can occur naturally in drinking water. A 1999 United States Environmental Protection Agency and Centers for Disease Control and Prevention on the health effects from exposure to high levels of sulfate in the drinking-water in two sensitive populations (infants and transient adults) did not show statistically significant effects.

2. *Non-dietary exposure.* Residential exposure could come from use of sodium bisulfate in consumer products, such as a toilet bowl cleaners. There are no risk concerns for these exposures.

D. Cumulative Effects JECFA (2010) confirms that bisulfate/sulfate anions do not constitute toxic metabolites. Thus, the Agency would assume that sodium bisulfate does not have a common mechanism of toxicity with other substances. As a result, any potential human health risks would be those that result only from the use of sodium bisulfate as a household use sanitizer for toilet bowls and as an inert ingredient in pesticide formulations applied to growing crops according to 40 CFR §180.920 applications.

E. Safety Determination

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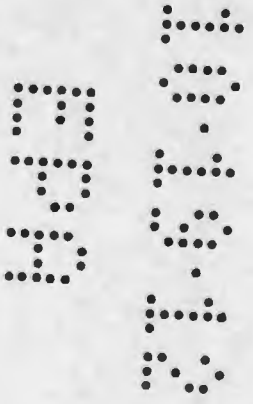

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October 19, 2012

PV Shah, Ph.D.
Branch Chief
Inert Ingredient Assessment Branch
Office of Pesticide Programs
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900 One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: Submission of EPA Pesticide Registration Improvement Act Information
Sodium Bisulfate, CAS RN 7681-38-1

Dear Dr. Shah:

Exponent, Inc. (as agent for Ecolab, EPA Company number 1677, 370 N. Wabasha St., St. Paul, MN 55102) is submitting Pesticide Registration Improvement Act (PRIA) fees for the following petition to request an exemption from the requirement of a tolerance:

- Sodium Bisulfate, CAS RN 7681-38-1, as an Inert Ingredient in Antimicrobial Formulations in Accordance with 40 CFR § 180.940(a): I003, $3,000, Pay.gov Tracking ID: 258B17RA, Agency Tracking ID: 74368196459 (refer to enclosed receipt).

This petition to request an exemption from the requirement of a tolerance for the use of Sodium Bisulfate as an inert ingredient in antimicrobial formulations, to include use on food contact surfaces in public eating places, as well dairy processing equipment and food processing equipment and utensils. The requested exemption would be listed at 40 CFR § 180.940(a) and is considered an I003, amend currently approved inert ingredient exemption from tolerance, no new data, PRIA review time frame 8 months, and a fee of $3,000.

If you have questions or need further information, please contact me at 202-772-4916 or cdaniels@exponent.com.

Sincerely,

Carrie Daniels
Senior Managing Regulatory Consultant
Exponent, Inc.

cc: Julie Spagnoli, Exponent
Ted Head, Ecolab